UNITED STATES OF AMERICA

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

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CENTER FOR TOBACCO PRODUCTS

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ELECTRONIC CIGARETTES AND THE PUBLIC HEALTH: A PUBLIC WORKSHOP

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PUBLIC COMMENT SESSION

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Memorial Sloan Kettering Cancer Center

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JIM BRAWNER
Cox Medical Center Branson

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NIMHD

M E E T I N G

(8:02 a.m.)

DR. DURMOWICZ: Good morning, and welcome back to Day 2 of our first workshop on e-cigarettes. I'm Beth Durmowicz for the Center for Tobacco Products, Office of Science.

Yesterday we addressed topics related to product science, specifically device design and characteristics, the chemical constituents of e-liquids and aerosols and toxicological considerations for these products. Today we will begin with a public comment session. In order to accommodate the great interest in participation, each presenter will be limited to a 3-minute presentation, and we will be using a timer.

After a short break, we will move on to sessions on potential performance standards, protective packaging,

environmental considerations, and considerations for chemical constituent and hazard labeling. Of note, in order to accommodate speaker travel arrangements, we will have the session on environmental considerations before the session on considerations for labeling. So this is a change in our agenda. We will only have panel discussions following the performance standards and environmental considerations sessions, but we will entertain clarifying questions for all sessions.

Dr. Carolyn Dresler will be our moderator again today.

Like yesterday, our agenda is full. Hence, our presenters have been asked to keep their presentations within the time period allotted, and a timer will be used in order to stay on schedule. We will have an hour break for lunch and end the day at 3:30. Please remember to bring all your personal items with you when you leave the room.

Similar to yesterday, if you have a clarifying question or a question for the panel, if you are on site, please write your question or questions down on one of the note cards provided, and promptly give the card to one of our volunteers in the room. If you are participating by webcast, you can e-mail your questions to our website, our e-mail address for

the workshop, which is workshop.CTPOS@fda.hhs.gov. The workshop is being recorded, and the transcript and webcast recordings will be posted on our website when they become available.

I would like to remind you of a few things from yesterday. The purpose of this workshop and this series of workshops is to gather scientific information about this novel category of tobacco products. This workshop is not intended to inform the Agency's proposed deeming rule, and we are not looking for advice or consensus, but are interested in an open exchange and discussion of scientific information. We request that all workshop participants be considerate and respectful of all other participants, the information being presented, and the opinions expressed by others.

The use of tobacco products is prohibited in FDA-occupied facilities, including the White Oak Campus. The policy applies to the use of all tobacco products, including cigarettes, e-cigarettes, cigars, pipes, chew, snuff, and dissolvable tobacco products. We ask that you respect this policy, as violators will be asked to leave the facility.

The restrooms can be found out the doors and to the right, and food and beverages will be served and available in the

reception area during the break and at lunch.

Please note that for any media inquiries, Jennifer Haliski is our press contact, and Jenny is in the same place as yesterday, in the back on the right.

And I would now like to turn the podium over to Dr. Dresler to begin our open public session.

DR. DRESLER: Good morning, and welcome back.

For those of you that were not here yesterday, I get actually the fun job of moderating and keeping everybody on time and working with the questions, et cetera. So that means keeping on time. So that said, we will be using this timer. And for those of you that -- you might be able to see green, yellow, and red. And on the facing part of it, it says how many minutes or seconds you have. So you all can't see that, but the speaker can. And know that when it's red, it goes to a negative number, okay? So this is letting everybody know.

We have a whole bunch of people trying to speak during the public comment session. We do have two hours for that. So you will know how over you are. I will know how over you are. And we are going to limit that amount of time, how long you are over, okay? So, please, please stay on time so we can be fair to everybody to get through.

So with that, I would like to welcome up the first speaker. I know that I see several of the empty seats of the speakers that aren't here yet, with traffic or whatever, and we'll add them into the end as they come. So come on up, and let's start.

MR. CONLEY: I am not Mr. Lauterbach. I do not have slides, though. Good morning. My name is Gregory Conley, and I am the President of the American Vaping Association, a nonprofit that advocates for small and medium-sized businesses in the vapor market.

Thank you for having me today. Before I begin, I must say that watching yesterday's presentation, I was disappointed in the level of scientific discourse displayed by some of the presenters who are anti-harm reduction and anti-vaping, as well as the inability of some independent researchers who have published some of the most significant work in this industry to give full presentations. As an organization, we agree that continued research into vapor products is necessary. We encourage this research. However, as we saw in 2009, when the FDA grossly misled the public of the NRT-like hazards of nitrosamines in e-cigarette cartridges in a study that continues to be used worldwide to justify harsh actions

against vapor products, such research becomes incredibly dangerous when it is spun to create the false perception of material harm.

The FDA's misrepresentation was one of the first in the United States, but it was surely not the last. Hype and conjecture surrounding e-cigarette toxicity has led us to a place where, in 2013, only 60% of the general public said that they believed e-cigarette were less hazardous than smoking. In 2010 that number was 80%. So 20 percentage points have fallen. And it is not because of a lack of regulation that less people believe e-cigarettes are less hazardous than smoking today. It is because of false claims made by those seeking harsh regulation.

Even worse, this research is hazardous from the onset when it's performed by researchers with little or no familiarity with the products and no desire to speak to vapers to determine if their study protocols are proper. At the present time, there is no generally acceptable way of testing e-cigarette vapor like there is cigarette smoke. As such, we find ourselves in a situation where researchers are presenting data on the toxicity of vapor products where they are improperly using the product, with unrealistic device settings

that no vaper would actually use. When relying on this evidence, and in this new and fast-growing field, the FDA should critically analyze each and every study and not just assume that passing peer review makes the study automatically acceptable to such an organization.

Importantly, we do not encourage more research because we fear that vaping may be more hazardous than smoking. Instead, we want to find out the relative risks of different classes of products, and in the process, we believe that all players involved should keep in mind that the hazards of these products must be compared to cigarettes, not no use of nicotine or tobacco at all. This is what the primary stakeholders in this dialogue, smokers and vapers, deserve. But, instead, they are being discouraged by a small group who are using falsely alarming language.

In closing, the greatest danger of these sorts of regulations is that the minute risks that we focus on often will actually lead to more smoking than we would have had without such regulation.

Thank you.

(Applause.)

DR. BANERJEE: Thank you very much for having me here.

I'm going to present results from a study that looked at advertising, print advertisements for e-cigarettes. We looked at two different classes of advertisements, implicit and explicit advertisements. And we wanted to see how do young adults, 18- to 25-year-olds, perceive harm perceptions and also their intentions to use e-cigarettes when they are -- when they see these advertisements for implicit and explicit ads.

Now, just to clarify, explicit ads are the ads that name the attributes of comparison, so tell you why e-cigarettes are different from conventional cigarettes, but also highlight the differences. So, for example, smoke-free, spit-free. The implicit ads, on the other hand, they name the attributes of comparison and claim that the product is better than conventional cigarettes or smokeless tobacco without really highlighting differences.

So some examples of stimulus ads. For explicit comparative ads were, for example, blu cigarette print ads, and for implicit one were Mistic cigarette ads, which were clearly showing that use of Mistic e-cigarettes is better, they are a better product than conventional cigarettes, but really not telling you why they were better.

The results clearly showed that for 18- to 25-year-olds, and we had about 1,000 non-smokers and non-tobacco users, they perceived the explicit comparative ads to be less harmful, that e-cigarettes were less harmful than regular cigarettes in terms of reducing tobacco addiction, causing tobacco-related disease compared with regular cigarettes. And they also had a higher intention to try the product in the next 6 months. And these were all significant findings.

So the conclusion is that e-cigarette ads with descriptors such as spit-free, smoke-free, freedom to smoke anywhere, they lead young adults to believe that e-cigarettes are less harmful than current cigarettes, and they report increased intentions of trying e-cigarettes in the next 6 months. So the implications of the study are -- and, again, I'm just presenting just a small data that was relevant to e-cigarettes -- that this increased scrutiny of e-cigarette ads is required, particularly ads that promote product as superior to conventional cigarettes, and also the necessity of including a warning label on e-cigarette packages and ads.

Thank you.

(Applause.)

MR. WALELE: Good morning, everyone. My name is Tanvir,

Senior Scientist at Fontem Ventures. And the title of my talk is Responsible Practice in E-Vapor Product Stewardship.

We've developed a comprehensive stewardship program to evaluate and assess e-vapor products. The program comprises three sections: premarket product stewardship, batch release, and postmarket product stewardship. The focus of this talk will be on pre- and postmarket product stewardship. Batch release will be commented on in my colleague's presentation.

Risk assessment is undertaken by registered toxicologists for ingredients and materials intended for use in e-vapor products. We use EP or USP standard nicotine and excipients to avoid potential impurities, such as TSNAs and diethylene glycol. As a minimum requirements, flavor ingredients are a food grade, and no CMRs or respiratory sensitizers are added. Materials which come into direct contact with the consumer, for example, the mouthpiece, have been approved for use in contact with food.

The quality tests we perform have been guided by existing regulatory frameworks, for example, the EMEA guideline on the pharmaceutical quality of nasal inhalation products and ICH guidelines for stability testing.

The potential for the inhalation of metallic components

used in the heating element and silica used in the wick is of concern to regulators. We have mitigated this risk by conducting exaggerating extractable testing. The stability of the e-liquid in terms of nicotine content and the identification of leachables have been tested under normal and accelerated conditions. We are aligned with the general consensus that a square-wave regime should be used to investigate vapor composition. A 55 mL volume and a 3-second puff duration has been used to benchmark our product to others on the market. To date, the focus has been on nicotine transfer and the quantification of carbonyls. Standard pharmaceutical tools, such as the Ames and IVM assays have been used to assess toxicology endpoints in vitro.

Fontem continues to monitor the long-term safety and health effects of its products once they are on the market. A dedicated customer service phone line is set up, and adverse event data is collected and continuously monitored. A risk management plan and detailed processes are in place in the unlikely event of a product recall. A number of chemical studies are being undertaken over the medium and long-term, and these have been registered on clinicaltrials.gov. Biomarker analysis is planned on urine and blood samples from

e-vapor users to compare against conventional cigarette users to identify potential perturbations in biochemical pathways. As part of postmarket product stewardship, Fontem will continue to use participation in industry meetings and forums to drive improvements, and welcomes the opportunity to work with regulators, such as the FDA, to contribute and shape future product and testing standards.

To finish, we believe our approach will provide reassurance to both consumers and regulators on the responsible stewardship and quality of e-vapor products.

Thank you for your attention.

(Applause.)

MR. FITZPATRICK: Good morning, ladies and gentlemen. I'd like to thank the FDA for this two-day forum and for offering this public session, comment session today. My name is Paul Fitzpatrick, and I'm the Program Manager for Quit Tobacco - UCanQuit2, the Department of Defense's tobacco cessation countermarketing campaign.

Like so many of us in the tobacco cessation field, I waited patiently and hopefully for the FDA to publish regulation on electronic nicotine delivery systems, commonly referred to as e-cigarette. While the April 2014 interim

regulation provides a framework for ENDS regulation, the FDA took a too conservative approach when it comes to ENDS regulation regarding advertising.

The federal court judgment of 2009 allowed the FDA to consider e-cigarettes a functional equivalent to traditional tobacco cigarettes. The interim ENDS tobacco regulation moves favorably in the direction in some areas but, in my opinion, falls somewhat short in the advertising part of the regulation.

The 1971 combustible cigarette ads were banned in -- against -- in 1971 combustible cigarettes ads were banned in TV and radio. Reducing public exposure in cigarette marketing helps deglamorize cigarette smoking, reducing the rate of smokers in America. Those cigarettes are still banned from TV and radio today. However, tonight you will be able to flip channels through your TV and find commercials for e-cigarette hawked by Hollywood stars, and you will likely have heard a radio ad for e-cigarettes during one of your two days of your drive here to this forum.

A new generation are being bombarded by sleek TV and radio ads for e-cigarettes, tempting these consumers to be cool and vape with their friends. If ENDS were only a recreational

device, this would not be an issue regarding the marketing of this product, but the truth is in their designation, as a nicotine delivery system. By function, design, and marketing, ENDS are intended to be one thing, to be a tool to create an addiction to nicotine for -- to enslave people to the addiction for nicotine.

The federal court has deemed that ENDS can be treated as the equivalent of combustible cigarettes. So I ask the FDA to extend this equivalency to TV and radio advertising. As the big three tobacco companies in America have moved to take over the ENDS market, it is clear that big tobacco sees ENDS as their conversion market to dual users and single-type vapor users, but they will have one thing in common: a consumer that is relying on the addition to nicotine to create their market.

So thank you for your time.

(Applause.)

MS. MOORE: Good morning. As you're aware, e-cigarettes are becoming increasingly popular. I'm here to talk about the potential environmental impact. A 2014 literature review noted that there had been little to no formal study of the environmental impact of the manufacturing process, use, or disposal of the electronic cigarette parts despite the fact

that many of these products are advertised as green or eco-friendly. Further, an earlier study reported that many of these products do not include instructions for proper disposal. At best, labeling in the industry is very inconsistent. Analysts predict millions could become litter on streets and inappropriately end up in landfills, similar to the amount of litter generated by traditional cigarettes. This will become increasingly problematic as use of electronic cigarettes becomes more widespread.

Electronic smoking devices have three main components: a cartridge which contains nicotine, a vaporization chamber, and a rechargeable lithium battery. The cartridge and battery pose a hazard to the environment if not disposed of properly. The batteries are considered e-waste, which typically cannot be disposed of by local sanitation departments. In some cases, when this e-waste is accepted, it is shipped to poor developing countries, particularly in Africa, where items are broken down and workers are exposed, as well as the surrounding air, land, and water, to toxic chemicals.

Lithium batteries are composed of a combination of toxic metals, such as lead, cobalt, and nickel, which tests demonstrated were leaking out in amounts that exceeded state

regulatory limits for hazardous products and pose a threat to both the environment and human safety. The U.S. Department of Energy's National Renewable Energy Laboratory has published material warning the public not to dispose of lithium batteries into landfills because of concerns that they may leak hazardous chemicals.

Lithium batteries are commonly found in household electronics, such as cell phones and laptops. However, the batteries in electronic smoking devices are not designed to last very long, depending on use and brand, and will be disposed of much more frequently than other consumer products. Also, because of their very small size and a lack of awareness regarding the potential dangers of lithium battery disposal, many people will simply throw them away with their regular trash. With the expected increase in sales, this could lead to an environmental crisis.

In response to this issue, several electronic cigarette manufacturers have started their own recycling programs. They vary widely. And while a company creating a recycling program is a positive step, it is a small one. First, it's unclear how many customers are aware of these recycling programs. Sometimes information about these programs is hard to find on

websites even when the company has them available. Second, there is no information regarding how many users participate in these type of programs. Will users be willing to save their used products for weeks at a time in order to mail them back when it's far easier and more like the habit most smokers currently engage in with respect to traditional cigarettes to just throw them away? Will they be willing to take multiple steps in some cases to send the cartridge to one place and the battery to another? Third, there are no guarantees that companies that operate these recycling programs will dispose of the products responsibly.

In response, there are several steps the FDA can take to address this issue at this stage. More studies need to be conducted regarding the environmental impact of electronic cigarette disposal and user participation in manufacturer-led recycling programs. And the FDA should require all companies to include information about proper disposal on all electronic cigarette packaging. The information should be prominently displayed at the point of sale and company websites. Finally, the FDA should require manufacturers to take additional steps to educate the public on the hazards associated with improper disposal through educational material and awareness campaigns.

These steps, taken now, can help address the large environmental problem before it becomes a true crisis.

Thank you.

(Applause.)

MR. SEGER: Hi. My name is James Seger. My company is E-Flowtech Research. I'd like to thank FDA and CTP for allowing me the opportunity to speak. I represent I am a one-man band small manufacturing company that is just starting up. I have pared my comments down to a few things I did not hear discussed yesterday.

First of all, advanced vaping equipment. Often, as advanced users progress through the devices from the starter e-cigs within a period of, you know, 1 to 2 years, they often wind up with much more advanced devices. I have one of these with me. If anybody would like to take a look at it, they're welcome to approach me, and I'll show it to them after.

These devices, the one that I have with me, flows approximately 950% more air than the standard RTA rebuildable tank device. This is an RDA, a rebuildable dripping device. These are so efficient that the users typically are using these devices at no more than 6 mg of nicotine because they're so effective at delivering them. The other difference is that

the more air-restricted RTA devices require the user to take a mouth to lung hit. This was not discussed yesterday. So they first pull, draw it into their mouth because it's so restrictive on airflow. Then they pull it into their lung, making it less effective on nicotine delivery, and I did not hear that discussed as far as being compensated for in the puff simulation models. These advanced RTAs, they take a direct lung hit. It's high velocity directly into the lung.

Another item I didn't hear discussed yesterday is I'm aware of approximately 100 known e-liquids, additives, and flavorings that cause a breakdown of polycarbonate, which is commonly used in the manufacture of these devices, the tanks and whatnot. And that breakdown of the polycarbonate could possibly introduce additional toxins to the vapors. So I would like to hear more research on that.

As a small manufacturer, I would like better access to research. I can't afford to click on a link and spend $60, $100 to read a paper that may or may not be pertinent to what I'm trying to discover. So that would be fantastic.

The last thing I want to comment on is clones and counterfeit materials. The RTA I have with me is a clone. It says made in USA in bold letters on the bottom. It is not.

It's made in China. It was $10. The insulator was made out of improper plastic. I don't know what kind, but it melted. It failed. It caused a battery short. I replaced it with an Ultem insulator. These clones look the same, but they do not perform the same. They're made out of sub-par equipment. They clone the e-juice, too. You know, American manufacturers are going to great lengths to make sure they're trying to provide a safe product. And you can go on madeinchina.com and punch in FDA-approved e-juice, and you'll get a bunch of hits. And they claim FDA approval. They also show forged FDA certificates. So that, in my opinion, is a grave danger that we face right now, and I am very concerned with the potential risk for DEG contamination because anybody can order any of the basic, you know, ingredients directly to their house right from China. And there's no reason to trust the USP certificates, you know, due to their track record.

Thank you.

(Applause.)

MR. GORE: Good morning. My name is Sean Gore. I'm the Chairman of the Oklahoma Vapors Advocacy League, or OVAL for short. Do e-cigarettes help smokers quit? Data shows pharmaceutical cessation products promoted by our health

agencies only have a 3% to 9% success rate. 60% are more likely to succeed using e-cigarettes or vaporizers. A recent study done by credentialed experts in Oklahoma indicates that a majority of vape store customers are exclusive e-cigarette users, at 64%, and not dual users.

Vaping does not present a health threat to bystanders. Peer-reviewed research, a study called "Peering Through the Mist" done at Drexel University reviewed more than 9,000 cases of e-cigarette usage and closely analyzed the vapor and liquids inside the devices. They concluded that the health risks were too low to be of concern for both puffers and people in their vicinity. Another study called the "Clearstream Air Study" conducted by Dr. Farsalinos concluded that it would be more unhealthy to breathe the air in big cities compared to staying in the same room with someone who is vaping.

Research shows e-cigarettes are vastly safer than smoking and pose no secondhand risk to bystanders. Smoking bans have largely been justified because of the risk posed to others by environmental tobacco smoke. Studies show e-cigarettes have no sidestream smoke. Evidence also demonstrates e-cigarettes are not a gateway to smoking. Research is not finding

e-cigarettes to be a gateway to smoking. In fact, it didn't seem as though it really proved to be a gateway to anything, says Theodore Wagener, Ph.D., Assistant Professor of General Community and Pediatrics at the University of Oklahoma Health Sciences Center, after surveying 1,300 college students. Another study conducted at Harvard titled "E-Cigarettes Not Gateway to Smoking" shows that, if anything, e-cigarettes are a gateway away from smoking.

E-cigarettes in perspective. For about 20% of smokers, none of the traditional methods of quitting work at all. They will lose years and possibly their lives due to smoking. According to the CDC, 480,000 Americans are projected to die from smoking this year. So we should keep our response to e-cigarettes in perspective and regulate as if the 500,000 lives matter the most and not the money.

So that leaves me with one last statement and a question. E-cigarettes are without a doubt the largest step forward in tobacco harm reduction we've seen in the last 50 years. So why are the FDA and the CDC-funded scientists falsely misrepresenting the data?

Just for short, this is my daughter's -- 4-year-old daughter's Orajel training toothpaste. The three main

ingredients, propylene glycol, vegetable glycerin, and flavoring, three of the main ingredients in e-liquids.

Thank you.

(Applause.)

MR. COHEN: I'm here today as the Head of Scientific and Regulatory Affairs at Ploom, Incorporated of San Francisco. In the course of my 3-minute talk, three smokers will die unnecessarily. That is the reality of today.

We wish first to comment that the field of vaporization includes a heterogeneous range of products. We believe that these rapidly evolving innovative products, especially innovation in devices, is to the benefit of the consumer if the devices meet appropriate quality and vapor testing standards, which may not necessarily require premarket authorization. Even yesterday we saw data being presented to FDA to guide future regulation from device platforms which are already several generations behind, and frankly obsolete.

If FDA is able to incorporate a continuum of risk approach to regulation of vaporization products as it has expressed an interest in doing, there is a great deal that may be accomplished. While we recognize the history that has led us to the regulation of tobacco, it is critical to continue an

open dialogue with all interested parties.

Over the past several months, I've been at eight separate meetings like this, including FDLI, TMA, and Morven. A key takeaway from me is that government, industry, and public health organization do have shared goals and interests that may be accomplished through effectively targeted regulation.

Ploom, my company, has invented and launched two unique vaporization platforms to date that heat tobacco leaf without burning it. Key assessments of toxicology and product performance have been executed, and we refer FDA and stakeholders to Ploom's comments in submission number 0189-79992 and wish those entered into the record. These data show that heating tobacco leaf through one of our platforms produces a vapor chemistry that is consistent with being less toxicologically harmful than conventional combusted cigarettes, which is important in the consideration of relative risk. In that testing, no significant increase above the negative control and no dose response was observed in the Ames salmonella mutagenicity assay, the neutral red uptake cytotoxicity assay, nor the micronucleus assay. Also, there was no carbon monoxide emitted, which is relevant in light of the comments of the delegate from the American Heart

Association yesterday who indicated that CO from cigarettes plays a causal and contributory role to cardiovascular harm. The AHA also stated that dual use may not reduce harm. Therefore, it is incumbent that future vaporized products be allowed to become sufficiently attractive to serve as a viable, harm-reduced alternative to cigarettes that will enable smokers to completely transition, not partially transition, completely transition from combustion to vaporization.

We also call on the FDA to consider imposing a standard that all pipes and hookah be carbon monoxide-free, because that is possible with the technology of today, right now. The same tobacco. A device has to change. That's all that needs to happen. It's very easy.

In summary, we at Ploom wish to productively engage with FDA so we can do the right things for our customers and for the broader public health. We welcome responsible standards and oversight that we hope and trust that this process will bring. We wish to thank the FDA and Director Zeller for engaging in an evidence-based and intellectually honest discussion to find the best path forward, which is appropriate for the protection of the public health. We thank you for

your consideration.

(Applause.)

MR. WILLIAMS: Hello. My name is Linc Williams. I'm the Secretary of the Board for AEMSA, the American E-Liquid Manufacturing Standards Association, as well as the Executive Vice President of NicVape, which is a e-liquid manufacturing out of Spartanburg, South Carolina.

I had planned this wonderful speech to tell people my personal story, but if you've ever been to one of these things before, everybody has heard that story of the transformation with my life. So, instead, I decided to -- I'd like to talk a little bit frank about what yesterday was like and extend an offer out to everyone in the room.

So yesterday was one -- first, it was a little invigorating, because 3 years ago the discussion was entirely about there was no science on these products, that they were entirely an unknown, that they were a fad, and that they were going to go away. And yesterday we started to hear public health experts as well as everybody across various industries and interests actually come out and say, you know what, there's no doubt that they are less harmful than tobacco cigarettes. So for me as a consumer, as well as in the

industry, that's a very refreshing thing to see.

The other thing that came up to note was the reliance on data that is 5 to 7 years old. The presentations we saw yesterday either unintentionally or intentionally chose to use data that is completely out of date based on technology. It's not even really used inside of the consumer industry anymore.

The other thing that was evidently clear is that there is still a clear lack of knowledge on how these products are actually used and what their performance capabilities and features are. So that gets to my second portion of it. Well, we've extended this out in the past, and I extend it out again. Any organization that would like to know how these products are actually used from the users and the manufacturers, we welcome you to contact us, to talk to us, because how these devices are used and how users currently configure them, which changes almost every month, is extremely important in understanding how to test these devices. So I extend that offer out to anybody from any organization to reach out to us, and we would be more than happy to help educate that process and truly understand it.

Thank you.

(Applause.)

MS. HAMMEL: Many smokers found out early on what was on the market at the time was not successful in helping them switch from tobacco. They innovated on what was available and produced the refillable tank systems and e-liquid into what has become representative of the small business owners you see today in vape shops. They have created countless jobs and even more success stories across this evolution. I believe it's imperative that you hear the numbers that have resulted due to this innovation and diligence.

We recently sent out an anonymous survey through a third party to thousands. And this is the result of that survey, which there are copies in the hall. Out of 2,049 respondents, 66% are over the age of 31. Only 14% were able to switch using a cartomizer type e-cig. If flavors were reduced to tobacco alone or tank systems were removed, 53 to 55% would go back to smoking or they would find another avenue. And a staggering 94.9% no longer use cigarettes and use an e-cigarette exclusively.

That is the result of the hard work and diligence we've done as small business owners. Cigarette innovation is unlikely, but vapor products hold the promise to harm reduction through innovation. As a small business owner in

the vapor industry, we now have eight locations and an independent mixing lab that is diligent in using safe manufacturing processes, testing, safe labeling and packaging, and know that the process of due diligence and practical safe manufacturing can be done within a small business.

We've also seen the results of this process and the impact it has made on our customers and know that it will help them switch successfully versus what has been offered in the past. What electronic cigarettes are to the industry and to the customers we see every day are nothing short of a miracle to them. What you may see as data and statistics, they see as a change of life and a necessary means of harm reduction.

But it cannot continue its rate of success if we go backwards in innovation. How can we be wrong when the survey numbers reflect all of what we are doing right? Based on these numbers, if we don't come to a solution for manufacturing versus removal or absence of open systems or flavors, 55% will go back to smoking cigarettes, and all of our hard work will be for nothing. I hope that you will consider these numbers and the impact that they've made to parents, grandparents, children, and grandchildren across this nation.

Thank you.

(Applause.)

MR. ELEY: Hello. My name is Scott Eley. I'm with NicQuid. I'm also the Vice President of the American E-Liquid Manufacturing Standards Association. I want to thank the FDA for the workshop and public comment period. I encourage the Agency to have more public comments opportunities given the extremely high interest in electronic cigarettes and vapor products.

As stated during the public workshop, initial studies are showing that vapor products are more successful in transitioning a user's dependence on combustible tobacco than prescription medications or NRT products. The scientific and empirical evidence has consistently found that e-cigarettes have replaced more than 3 billion packs of cigarettes worldwide in the past 7 years, have helped several million smokers quit smoking or reduced their cigarette consumption, are more effective than FDA-approved NRT smoking cessation products, which have a 84 to 95% failure rate, pose fewer risks than FDA-approved Chantix, have never been found to be a gateway to smoking, cigarette smoking, emit trace levels of nontoxic aerosol that pose no harm to nonusers, and have

further denormalized cigarette smoking, as youth and adult smoking rates and cigarette consumption have declined every year since 2007, when vapor sales began to skyrocket.

I very strongly encourage the FDA to reevaluate the currently intended application of $275 million set aside for e-cig and vapor product research. Youth experimentation is common with many substances. The CDC survey of youth ever try misrepresented data by including those who indicated they would consider trying and those who have merely tried the products under the category as user of the products. And year over year, data indicated the only increases were amongst those identifying themselves as smokers.

Resources targeted to build a virtual convenience store targeting 13- to 17-year-olds to assess how e-cigarette displays and pricing affect the tendencies in minors to buy the devices could better be spent on verifiable and scrutinized real science especially considering that 41 states already have laws banning the sale to minors and many other states have bills planned in 2015. $2.7 million the Agency gave to a group to monitor Facebook posts to determine how people modify devices is also wasteful, as the results would be outdated before the study even concludes. Verifiable and

professional scrutiny through the process of peer review and publication should be the policy for all research, including any and all funded by the FDA and taxpayer.

I and millions of other former smokers around the world embrace these alternatives while tobacco cigarette sales are simultaneously falling. We all agree reasonable, realistic and sustainable regulations are needed to establish consumer protections and good product stewardship, but without devastating a multi-billion-dollar industry and/or eliminating viable and effective options for both current consumers and current smokers.

Thank you.

(Applause.)

DR. POLOSA: Good morning. My name is Riccardo Polosa. I am Professor of Medicine at the Catania University in Italy, and I declare this conflict of interest.

But first and foremost, I'm a doctor, a doctor engaged with real smokers and real patients with smoking-related conditions. My research team has been performing clinical behavioral research with electronic cigarettes since 2009 and has published more than 20 peer-reviewed articles on the topic. My purpose in being here is to outline a few recent

key observation that FDA officials may consider in their effort towards a sensible regulation.

In the U.K., but also in France as well as the U.S., where electronic cigarettes have been allowed to be marketed as a consumer product, substantial have -- benefits have been observed. Most important of all, smoking prevalence has declined. Unquestionably, electronic cigarettes are not renormalizing tobacco smoking in countries where a liberal approach towards these products has been adopted.

Systematic reviews and meta-analysis now suggest a strong positive association between electronic cigarette use and smoking abstinence, with an average quit rate of about 20%. This is a collateral benefit for many smokers switching to electronic cigarette use. Please note here that up to two-thirds of smokers who successfully quit tobacco by switching may end up quitting electronic cigarette as well. This has been little studied in current surveys especially, but it is an additional mechanism by which electronic cigarette may contribute to the observed decline in smoking prevalence.

Emission data indicates that electronic cigarette toxicology is by far less problematic than combustibles. This

favorable profile has been also recently confirmed in the urine of regular single users compared to smokers. Much of the current research unfortunately focused on the potential harm of these products when, in fact, there is emerging evidence pointing to the beneficial effects of electronic cigarette use both in health and in disease. For example, inviting smokers with elevated systolic blood pressure to switch to an electronic cigarette can substantially reduce their blood pressure. Further evidence for harm reversal is coming from asthmatic smokers. Regular electronic cigarette use -- and subject asthma --

This is the last one. And I don't think it needs to be a daunting task after all. But we should focus on quality, safety product standards, and carefully monitoring smoking prevalence nationwide.

Thank you.

MR. ROWBOTHAM: Good morning. I'm Andy Rowbotham. I'm a member of the management team responsible for the manufacture of electronic vapor products, or EVP, at Fontem Ventures.

At Fontem, we believe we bring lots of things to the EVP sector, with the most important of these being quality, responsibility, and integrity. This is a time of change, when

the medical community increasingly seems to be reaching consensus that not only are EVPs relatively safe, but they could also present potential health benefits to migrating smokers. We believe that during this time of change, quality will become the single most important development in the industry and that regulation must help to establish the quality standards which guide EVP manufacturers' activities and protect the consumer.

We've been leading the cause for standards and for fair and proportionate regulation so that we can educate the interested user and, as safely as possible, deliver the experience that they deserve. Today we want to explain the quality manufacturing approach we use for our products so as to give you an overview of the kind of requirements and standards which could be applied across the board.

Our manufacturers operate far and above the minimal standards in which many EVP products are made today. We consider this as an obligation to the user, not a choice for the manufacturer. Fontem's total quality manufacturing approach encompasses our whole business. Business quality ensures we have a reliable, sustainable, and secure environment without the risks presented by unacceptable

business practices. Manufacturing quality ensures that product manufacture takes place under strict controls with high levels of component, incoming quality control, standard operating procedures, on-the-line supervision, and finally, the routine testing of every device.

Liquid manufacture using European Pharmacopoeia nicotine and excipient source from reputable suppliers is done in clean room type conditions in our U.K. manufacturing facility. And product quality ensures that our products are designed and manufactured to the stringent requirements we believe our consumers deserve.

We chose an FDA-inspected ISO 13485 certified manufacturer of medical devices in China to make our devices. Mixing, filling, and packing is carried out in the U.K., where we currently operate in a facility certified by the MHRA. The products we manufacture and these suppliers are specified to high safety standards. Quality specialists and scientists mandate our quality testing requirements through manufacturing service agreements, associated technical agreements with our suppliers. The testing regimes and procedures such as those you see on the screen ensure that every batch is tested before being released onto the market.

Our vision for the future and for future regulation would be as follows: Automation will further enhance product quality through increased consistency and improved hygiene. Food-safe coatings and child-resistant packaging will be standard when risk assessment shows they're required. Automated testing will ensure that all products work without leaking or overheating and produce an acceptable vapor. Products will be traceable back to component level.

At Fontem, we believe the manufacturing standards I've talked about should be applied across the global supply chain. We hope this short insight into the Fontem total quality manufacturing philosophy illustrates what we mean by quality, responsibility, and integrity.

(Applause.)

DR. ZIMMERMAN: So good morning, everybody. My name is Ralf Zimmerman. I'm coming from Rostock University, and we are doing their research on online measurement of tobacco devices, and also, we have a spin-off company who is building measurement devices for that purpose.

So our technique involves photoionization mass spectrometry to online and puff-resolve measured as the compounds, toxicants from cigarettes, but also e-cigarettes

and heat-not-burn devices. And we think that the smoking behaviors or the actual puff profile is very important to address the specific effects here. So online measurement, I think, matters. And the smoking device design and the manipulation of the devices can -- very well addressed by this technology.

So we use light to ionize and have soft ionization so we can see the profiles of the toxicants directly online, which, of course, allows us to compare different devices. You can see just a glimpse of different cigarettes, conventional cigarette and a heat-not-burn device, and e-cigarettes. And in the higher mass range, where we have the toxicants, we have a very clean spectra here for these typical e-cigarette types. So the risk seems to be very, very much lower by orders of magnitude if you consider the toxicants of these compounds.

And, of course, we can do the measurement then online, so puff by puff. And this is very much dependent on the actual puff profile. So we have to consider that for regulation that we see the real smoking conditions, how these compounds are formed, because it makes a big difference.

If you now look at different devices, we can see, in this case, for nicotine, that we have a different behavior of

release. If we have a charcoal heated heat-not-burn device, we have this bell-shaped release curve. So each peak is a concentration of nicotine here. E-cigarettes have constant release, but normal cigarettes typically have a linear increasing behavior. And some vendors now try to copy this, and they have like a pod heat-not-burn device, so they try to mimic this behavior release, so to have the same feeling with -- like with e-cigarettes. So it's very important to have the puff resolved information here within this type of devices.

And another important point is depending on the smoking conditions, we can measure toxicant, like here polyaromatic compounds in e-cigarette smoke. And depending on the conditions, it can happen that we have PAH formation to pyrolysis, which we can see here puff by puff, as well -- like with the nicotine.

I would like to summary: The important point is that more research is also available for small companies and universities to look at these effects and then more realistic conditions. Don't let us do the same mistake like with ISO profiles, which say nothing about the real risk of cigarettes because it underestimates the risk by far.

Thank you very much.

(Applause.)

MS. HOKE: Good morning, everyone. Thank you for the opportunity for the Tobacco Control Legal Consortium to offer public comments here today. While the Legal Consortium is concerned about a variety of different policy issues related to the regulation of e-cigarettes, including flavors, warnings, advertising, and youth access, today we'll focus on child-resistant packaging for liquid nicotine.

As we all know, the e-cigarette marketing, or market, is expanding greatly and changing also, as you've heard from several people today. One of the consequences is we're seeing more of the refillable products, and also then more of the liquid nicotine that's used to refill those products available in a variety of different sizes of products and different levels of nicotine. We know and have known for a long time that nicotine can be deadly. It can cause illness. The threshold for consumption of nicotine is not exactly known, but somewhere between 1 and 3 mg of nicotine per 1 kg of body weight.

That might not really make sense to anybody, but let me put it in real-people terms. My granddaughter is 17 months old. She weighs 20 pounds. If she were to ingest a vial of

sweet, cherry-flavored liquid nicotine in the traditional size that you can find, she would assuredly become very ill and could, in fact, die. In fact, just yesterday in Fort Plain, New York, a child died after ingesting liquid nicotine. So this is a real problem.

We're seeing escalating reports to poison control centers around the country from children, young people, ingesting the liquid nicotine. In 2011, about 270 calls to poison control centers. Already in 2014, over 3,300 of these calls. So the problem is real. The question is what's the solution.

Several states or many states have considered legislation that would impose child-resistant packaging. Minnesota, Illinois, and Vermont have done so. But we all know that the comprehensive federal approach for this particular issue will be better. What could the FDA do? First, the FDA could adopt a product standard under Section 907(a)(3) imposing child-resistant packaging. That's a lengthy regulatory process. We understand that. But certainly the FDA has done that with other products, over-the-counter medications and the like. And so there's a history and the capacity to do that in collaboration and using the resources of the CPSC to help in that regard.

The other thing that the FDA could do, however, is when implementing the deeming regulation, they've indicated that they're going to give a 24-month window for new product applications to be filed while the product can still be marketed. That will apply to electronic cigarettes. That could simply be amended and allow only the products that meet child-resistant packaging standards to be marketed during that 24-month window.

Thank you.

(Applause.)

MR. MARSHALL: Good morning. My name is Jack Marshall. I'm the Director of Communications and Training at Altria Client Services. Our team provides regulatory support on behalf of a number of our operating companies, including NuMark. As my colleague, Dr. Flora, mentioned yesterday, NuMark markets e-vapor products in the United States under the brand name MarkTen. Earlier this year, NuMark acquired Green Smoke, and it's Green Smoke e-vapor brand. We appreciate CTP organizing this workshop and providing a constructive forum in which industry, academic researchers, and FDA can share information on the important scientific issues related to electronic cigarettes.

In addition to our participation at this workshop, we look forward to participating in the subsequent workshops that CTP has said it will hold on the individual and population health effects of e-cigarettes. Each of these workshops can help contribute to a transparent and science and evidence-based discussion about the importance of a comprehensive tobacco harm reduction strategy.

At Altria, our framework for tobacco harm reduction has many facets, including communicating tobacco health effects, supporting underage tobacco prevention, and providing cessation support to help adults who make the decision to quit. It also includes developing potentially lower-risk products. As manufacturers of tobacco products for adult consumers, it's important that we continue to understand evolving consumer expectations. Our data shows that greater than 50% of current smokers are seeking alternative tobacco products. And most within that 50% are not necessarily interested in traditional moist smokeless tobacco products. It's this adult consumer interest and feedback that informs our product development efforts.

To achieve tobacco harm reduction, any potentially lower-risk products must be acceptable to adult tobacco consumers.

It's important for this harm reduction strategy to focus on creating and recognizing innovative products that can reduce harm for smokers. E-vapor products, which have grown considerably over the last few years and have been the topic of this workshop, are a good example of this kind of innovation. A few months ago, FDA proposed its deeming regulations to pull in most other forms of tobacco products under its regulatory authority, including e-vapor products. In doing so, FDA recognized the potential of harm reduction and the concept of a continuum of risk. To the extent FDA can implement a comprehensive tobacco harm reduction strategy, it will be among the most effective and meaningful actions FDA can take to reduce the health effects of tobacco use.

We hope to continue working collaboratively with members of the public health community and FDA to achieve tobacco harm reduction over time. Workshops like the one taking place here are an important part of that process.

Thank you.

(Applause.)

DR. AGUIRRE: Good morning. So I'm a very unlikely presenter, because up until 2 years ago, I had no idea about any of these things. But I'm a child and adolescent

psychiatrist at McLean Hospital. I treat very self-destructive adolescents that are almost tautological. But three things got me here. One was the observation that increasing or ongoing numbers of adolescents were coming in with smoking, and the other thing was that my godfather died of lung cancer. But the thing that got me was when my cross-country running son brought home a pack of e-cigarettes and regular cigarettes that his friends had asked him to hold for him [sic] so that they wouldn't be caught. So I got to start thinking about this and then found these -- the data online that 3,200 kids try cigarettes every day and that 2,100 regular -- people who smoke occasionally become regular smokers.

So in our unit, we were trying to use lozenges and gum to stop people from smoking, and generally, the adolescents would tell you what you could do with those lozenges and gum. And I said, well, that's not really the way that they're supposed to be used. But they were interested in electronic cigarettes, which was sort of interesting to me. So I thought, okay, well, in terms of a harm reduction, and I was just thinking about the many small companies that are trying to bring their ideas, that if we allowed electronic cigarettes and these sort

of things to be more regulated than traditional tobacco products, that it would hand big tobacco a huge victory, because they've got such massive resources compared to a lot of the small companies, and again, hand them these 3,200 smokers a day that could potentially -- that aren't interested in gum and other things like that. So, you know, obviously, everybody has been saying this, and you know, the other thing was with advertising and sales. It really ought to be regulated in terms of selling to people under 18.

So what I think from my perspective is just that, again, the quality of the product. I mean, I think a lot of people cut costs, and then you get all these sort of studies that show that there's 10 times more carcinogens. I think that these, they really need to be regulated. Testing must be done for content. And the FDA should be very explicit about advertising to minors.

And I leave you with this thought experiment. And I'm a father of four adolescents, and that's why I'm here, because I run away from them. But, anyway, but if that 16-year-old son of mine were to be smoking, I would want him smoking a well-regulated electronic cigarette rather than a cigarette each and every time. And if this were your children, you know, and

you were caught with this, you know, what would you do?

So thank you.

(Applause.)

DR. BURSTYN: Good morning, folks. First, a small correction. Actually, my affiliations are on this slide now, not from the previous introduction. So slight substitution in the program.

So what I'd like to talk to you about today very briefly is that there's really not that much new about e-cigarettes. I don't come from the tobacco control world. I come from a very different area of academia and research. And I was surprised that so many things about electronic cigarettes were surprising to people. So that's my story.

So we're really not all that ignorant about toxicology of what comes out of electronic cigarette. And I talk about it as somebody who is trained in industrial hygiene and environmental health who was taught to anticipate what would happen if my workplace had a source of environmental emission introduced to it that was very much like a electronic cigarette and it was there and it was exposing me. And I was trained through my undergraduate and my graduate training to recognize and deal with those situations and be able to make

rational decisions about mitigating risks for myself and my coworkers and my colleagues.

So we have rich experience from other areas of environmental and workplace emission controls and hazard assessment that are incredibly helpful and can be easily applied and are portable to the world of electronic cigarettes and tobacco products. And there's really no reason to assume this precautionary posture that really amounts to willful ignorance. We really know a lot more than we sometimes give ourselves credit to. And my cred, such as it is, is summarized in this paper, and if you're really interested in what I have to say on this topic, it's all published out there. You're most welcome to contact me. I am easily found.

But this is my main point, which was made yesterday as well: Dose makes the poison. We knew that for a very, very long time, and it's really not helpful for us to think otherwise, because nothing really has changed to the truth of that statement since Paracelsus put it forward.

And this is part of the story. If we apply standards that are admissible in the workplace as to emissions from electronic cigarettes, and we look at about 9,000 chemical measurements that were available to me back last summer, we

can see that across chemicals, we see individual exposures that are way below a threshold where we would actually begin to worry about them. There's really no reason to be concerned here. Most of them are in trace quantities. They're present, but they're not going to hurt you.

And if you look at the similar calculations based on emissions from vapors, you can reach the same conclusion. You can sit or stand near vapor and experience the sidestream emissions, and you should not be worried, afraid for your life or health.

So we do know a great deal about electronic cigarettes. If the word "cigarette" was not in that title, we wouldn't really be that worried about them because it's just a name. And it's not really appropriate to deal with these things as if we've learned nothing since the 16th century. Scientists don't turn away from vials of chemicals, and neither should the public. We should understand them and treat them with respect, but we should not be afraid of them.

Thank you very much for your attention.

(Applause.)

MS. O'DAY: Thank you. COPD is short for chronic obstructive pulmonary disease. It's a umbrella term that's

used to describe progressive lung disease. It includes emphysema, chronic bronchitis, refractory asthma, and severe bronchiectasis. And it's most often associated with tobacco smoking. The COPD foundation is a not-for-profit organization established to undertake initiatives that result in expanded services for COPD and improve the lives of individuals affected by COPD. Our activities focus on achieving these results through research, education, and advocacy programs.

I am Miriam O'Day, and I have no conflict of interest. I am a consultant to the COPD Foundation.

The growing popularity of electronic cigarettes is a cause for concern to the COPD Foundation. We don't know whether e-cigarettes have an overall positive or negative impact on public health. It's been claimed that e-cigarettes offer a healthier alternative to conventional cigarettes and can help smokers overcome addiction. However, they pose risks of their own, such as poisoning, and we've heard much of that today. According to the CDC, the calls to poison centers have increased significantly, from about one per month in 2010 to about 215 per month in 2014. There is also the possibility that e-cigarettes are taken up by those who would not have smoked otherwise, and we just heard that from the previous

speakers.

A study from the University of California at San Francisco found that adolescents who used e-cigarettes are more likely to smoke conventional cigarettes and less likely to quit smoking. The study also found that e-cigarettes are among the middle school and high school students -- they double their risk between 2011 and 2012. So we're especially concerned about the way that e-cigarettes are being marketed to young people, being produced and advertised, and in candy and fruit flavors, etcetera.

So what we are calling for is more research, identifying the impact on people with existing lung issues, determining the role in long-term smoking cessation and whether it differs in people with existing lung disease, understanding the impact of secondhand smoke and the exposure to vaping or vapor. We want the focus on minors, the enforcement of sales restrictions to minors to be very tight to create stricter regulations for marketing, to limit the use of flavors, and to control labeling.

So thank you very much for your allowing us to make comments today.

(Applause.)

DR. NITZKIN: Thank you. My name is Joel Nitzkin. I'm a public health physician. My travel here is supported by the R Street Institute. The opinions I express here are entirely my own and have not been reviewed or influenced in any way by R Street, the American Association of Public Health Physicians, or any other organizations I am or have been affiliated with.

My presentation today is based on the chemical similarity of e-cigarette fluid and the pharmaceutical nicotine replacement therapy products, the patches, gums, lozenges, nasal sprays, and inhalers. FDA considers these products safe for general use without restriction as to dose or duration of use. With FDA approval, they are sold on open shelves in a variety of fruit and candy flavors. I urge CTP, the Center for Tobacco Products, and TPSAC consideration of tobacco harm reduction. This topic fits today's agenda as well as it fits the agendas of the next two FDA e-cigarette workshops.

Tobacco harm reduction means informing smokers that they can reduce their risk of potentially fatal tobacco-related illness by 90% or more by switching from cigarettes to a smokeless or vapor alternative or by using a pharmaceutical nicotine replacement therapy product in a long-term basis in a

harm reduction mode. A tobacco harm reduction initiative, if added to current tobacco control programming, could secure personal and public health benefits not otherwise obtainable. Even a modestly successful THR initiative, if added to current tobacco control programming, could avert the deaths of two million of the more than eight million Americans projected to die of a cigarette-attributable illness over the next 20 years. A highly successful initiative could save double that number and reduce the number of American smokers by 90% by 2035. I know of no other tobacco control policy option that could secure this level of public health benefit.

In addition, experience today has shown that e-cigarettes can be marketed in a way that attracts smokers to switch without attracting nonsmoking teens to continuing use. Center for Tobacco Products leadership, CDC, and the Surgeon General all recognize the continuum of risk. All recognize the potential personal health benefits of switching to e-cigarettes. Despite this, the Center for Tobacco Products seems not to have considered how such benefits could be secured in either the CTP research agenda or the proposed deeming regulations.

I therefore urge the Center for Tobacco Products to play a

lead role to determine the set of tobacco control policies and FDA regulations that would best enable us to capture the personal and public health benefits tobacco harm reduction can secure, and do so in a manner that will minimize, if not totally eliminate, potential adverse effects related to initiation and quit rates.

If in the opinion of FDA leadership this cannot be done without amendment of the FDA drug and tobacco laws, I urge the Center for Tobacco Products to work with public health industry and consumer stakeholders to secure the needed congressional action.

The review I recommend should determine -- oh, okay. Let me stop there then.

MR. BRAWNER: I'm Jim Brawner. I represent Cox Medical System in southwest Missouri. I am a tobacco treatment specialist, and I have had over 130 complete the program going through that -- through the Cox Medical System. We have, of those participants, about 36% who come into the program using the electronic cigarettes. We only recommend the seven approved nicotine replacement therapies currently, but I sincerely believe there is future hope with the electronic cigarettes to contribute to the cessation process in those

individuals.

The problem that these participants are experiencing when they are trying these devices, the closed system has worked better. They're purchased from a big box discount store; in the open system, from a vapor store. The participants' main comments about the devices were that there was more consistency within the closed system, as it has evolved, in their case. The open systems were not easy to draw. They're too large, in most cases, and to get a seal, too much vapor-causing cough. And within the system, categorized the experience, only one out of those 36% said that these were truly satisfying on a scale from very satisfied to very unsatisfactory.

Also, in our area, I have a survey done, 50.1% in a group of 11- to 13-year-olds had parents that either used the electronic cigarette or some tobacco product. Of that population, 14% were currently using the electronic cigarette. My caution would be to ban that advertising extension to include these products until we can come to a better conclusion.

The new data also in our counties, we have a high rate in the twin counties in southwest Missouri, the highest rate of

pregnancy use of these devices and smoking in the state of Missouri. So it's been a great process and educational process for me to really understand. And Miriam O'Day, I want to ditto her comments. COPD, I have many in those classes, and they have tried to use these devices. The more we can get these regulated and understand that our consumers are who matter here.

Thank you.

(Applause.)

DR. CHOI: I'm told to wait. You can stare at me if you want.

(Laughter.)

DR. CHOI: Or you can check your e-mails if you want to.

(Pause.)

DR. CHOI: Okay. Now that's me. So let's move on to the first slide. This is my disclaimer, and basically, it's saying that if you have any problem with what I'm going to say, come talk to me. Don't call my boss.

(Laughter.)

DR. CHOI: And also that I'm an intramural investigator at NIH. That means I have no inference on a funding opportunity -- and part of NIH and FDA CTP, and I do not manage any of

those grants. So that being said, I want to provide a few perspective for us to think about before we continue with the second day of the workshop.

So, first, what should we compare to when we evaluate e-cigarette? We're talking about the product safety and evaluation of it. A lot of research conducted to date compare e-cigarette to cigarettes and found that e-cigarettes are "safer" than cigarettes. Now, however, at a population level, almost everything is safer than cigarettes. Texting and driving is safer than cigarettes. It kills less people than cigarettes. Crashing a Boeing 747 every day for a year kills fewer people than cigarettes. So we use cigarette as the safety standard. I think that's way too low a bar. And for products that pass that standard could still do potentially great harm in the population.

Now, then, the question is what should we compare it to? Should we compare it to a nicotine inhaler as the standard, given it's kind of a product safe to be used for smoking cessation? I leave that for all of you to think about.

Second, there was some discussion yesterday about comparing e-cigarettes and medication or medical devices, particularly speaking about the medication -- in the market

before. The long-term risks are being evaluated. However, there is a fundamental difference between medication or medical devices versus electronic cigarettes. Medications and medical devices provide benefit in spite of the risks, potential risks that are involved in those medications, versus e-cigarettes if used continuously, at its best, provides harm reduction.

The analogy I would make is that it's like you don't owe any money, but you go to a bank to get some -- get a loan versus you already owe money, but then you get a loan reduction from the bank. In the first case, you have cash in your hand. In the second case, you don't. There's a qualitative difference in those two situations. I would say the qualitative difference also exists between medications and electronic cigarettes. So in that case, risks associated with e-cigarette use should be carefully evaluated and maybe to a greater extent than medical devices or medications. Just a suggestion.

Third, how user use of electronic cigarette matters. So this diagram, this one, shows that -- the red line shows young adults who did not use e-cigarette at baseline, follow-up for a year. They show a significant reduction in cigarette

consumption. Now, the blue line represents those who currently use e-cigarette at baseline, and a year later, they have a slight increase in cigarette consumption. Now, we can all speculate why that happened, but one of the things that's possible is that the user behavior or how they use the product is not actually helping them to reduce their cigarette consumption.

So one way to deal with it is that if we can regulate and standardize the use behavior through product -- that may be able to help and make the product actually helpful in helping people to cut down their cigarette consumption.

Thank you.

(Applause.)

DR. DRESLER: I am not seeing anybody else in that next speaker seat. So that means we have completed our speakers for the public comment session. Thank you very much for coming and giving those presentations to us.

It is now time for a break, and so because we are a little bit ahead, that might mean we have longer for lunch or longer later in the day. Let's still go ahead and stick with our 15-minute break, please.

As Dr. Durmowicz said, if you would like, the restrooms

are out to the right and around the corner, and there is a kiosk there for drinks or snacks, all right? We'll be back here, let's say, in 15 minutes, let's say at 20 till, okay?

Thank you very much.

(Off the record at 9:23 a.m.)

(On the record at 9:43 a.m.)

DR. DRESLER: Okay. Thank you for reconvening, and it's wonderful how quiet you've become so quickly, so thank you.

Our first session for this morning after the public comment session is on Potential Performance Standards, and our first speaker is Dr. John Lauterbach from Lauterbach and Associates, speaking on Keeping It Cheap and Simple While Others Call for Costly Complexity.

Dr. Lauterbach?

DR. LAUTERBACH: Okay. Thank you very much. I'd like to thank the FDA for holding this workshop and accepting my abstract for presentation. I'd just like to touch base on a couple things that -- from yesterday's meeting particularly dealing with first formaldehyde. The -- chemists of the group report the results of their assays as formaldehyde. What we don't know for sure, particularly in a high glycol, high water environment is that formaldehyde there is formaldehyde gas or

is other hydrated species, such as methylene glycol or other oligomers of formaldehyde combined with water. So just please remember that. Also, please remember there's a great wealth of data under all sorts of smoking conditions out there in the literature on formaldehyde deliveries and other carbonyl deliveries from conventional cigarettes under all sorts of smoking conditions.

The second follow-up from yesterday is that there was questions on mixture toxicology. There is a tremendous amount of inhalation toxicology in supporting chemistry and in vitro toxicology on flavors and flavor mixtures in the literature. It's very easy to find.

Third, Lauterbach & Associates, that's my company. We're paying our own way here. Our business, basically, is we help small tobacco product manufacturers who are now also getting into the e-cigarette business meet FDA regulations. We've been in business now for 10 years, and I have three associate scientists that help me from time to time.

Okay. What we're heading for on this presentation today is to take a look at some very recent toxicology studies on the cigarette-like e-cigarettes, not the tanks, not the bazookas, but basically things that I buy at my local

convenience store. We always talk about Apple technology. That's some of my original background. I want to show some things that basically can help out on this area, but they're not total solutions. We'll discuss some of the things dealing with hazards versus test complexity, particularly covering on if the test is going to tell us anything, and like so many other tests that we've had in the cigarette industry, do they really tell us anything that we don't know already? And, finally, that line of approach which basically is minimal testing and resulting in minimal hazard by more of a consensus standard approach.

Now, just for everybody's clarification here, there's four recent studies in the peer-reviewed literature, the first one by Steve Hecht on basically urinary biomarkers of smokers. And most of these smokers were basically tank systems. They did have other with the cartomizers, the disposables. Basically, again, very low levels of biomarkers associated with metabolites of pHs, acrolein, whatever, TSNAs versus conventional tobacco products.

And then we have the three papers from Lorillard, some of that you saw yesterday afternoon in Bob Leverette's presentation on in vitro toxicology, another paper on

basically e-cigarette aerosol chemistry, and the third one dealing with exposure to bystanders. All these are, I believe, open access literature, including the one in regulatory toxicology and pharmacology. That's a very interesting paper if you're ever concerned about deliveries on the cigalike products, okay?

But basically, taken together, it says that we have a class of products that is very low in hazards compared to conventional cigarettes. These, again, are talking about commercial products. Some of those you saw pictures of in the presentation yesterday afternoon. And I think the bottom line here is, at least for one class of e-cigarettes, we have a product with such reduced hazard that we need a different regulatory approach.

Again, as we go through our thoughts on testing, we have to have meaningful testing, it must be affordable, and it must produce timely results. If the test takes three months to complete, that's not going to be very helpful unless we're talking about some basic research such as inhalation studies. I mean, it must be -- if we're going to measure something here, the dose makes the poison was mentioned earlier.

We know that many laboratories can find very trace amounts

of things in tobacco products and other consumer products, in air, whatever. I get every year or so something from the Macon Water Authority -- live in Macon, Georgia -- telling me all the trace contaminates in the drinking water, but it still passes U.S. EPA requirements. But nobody seems to get concerned over trace amounts of things, but they're there, because most of these results are below levels of toxicological concern, whether it's in vegetables, which have a whole host of heavy metals in them from where they're -- the soil their grown in, water, runoff. Everything else out there has some levels of contamination, but they're all -- below the levels of toxicological concern. So the question comes in: Can we really look at the same thing in terms of e-liquids and e-cigarette aerosols?

Now, we talked a little bit about testing. A lot of people would like to put a tremendous amount of testing into this product, okay? And I realize if I were on the other side of the fence with a great laboratory to run, I'd want to test everything, too. It's job security. Just an example here of a software that helps people get through some of the analyses, but again, it helps give them -- you know, on some of these mass spec identifications -- I'm trying to get a mouse here,

and I went backwards -- but this gives you some better information about some of the mass spec identifications. Obviously, nothing substitutes for great chromatography and a whole bunch of standards.

Now, another project we've been working on with Dr. Andrae Spencer over in Wilson, North Carolina is looking at sources of carbonyls from PG and glycerin, particularly formaldehyde, acetaldehyde, and acrolein. We've been using carbon-13 labeled product, and that allows us to say what's coming from the glycerol or PG versus what may be coming from other points in the device, such as outgassing of polymeric materials, et cetera.

And just a brief outline of what we've done. We started this work earlier in the year. We basically have gone to a more refined thing with larger amounts of label used in the cartomizer. At 10 drops, you could always say, well, maybe we're pyrolyzing things. Again, we've -- working somewhat 55/30/3 profile to 55/2/30 again. And, again, puffed until there is no visible aerosol, again, using the standard carbonyl procedure. Again, please remember that anything that could be a hydrated carbonyl and stay hydrated under actual human use is going to show up as formaldehyde.

This gives again a summary of some of our results. I call your attention to this last point. Yeah, we did find a high level of formaldehyde, about a microgram per puff, but this was an anhydrous system. If you notice, a lot of the e-liquids have water in them, and we don't have the results to report today, but adding water to the e-liquid reduces its tendency to form carbonyl compounds.

So where are we? We can test a number of things. We have to ask our question. Will a very extensive testing regime improve overall public health? Will it improve the health of the e-cigarette users or their bystanders? Will it allow a clear distinction between what's good and what's bad? Is it going to be practical to administer? How many toxicologists do we have out there to review data from every single vape shop that's doing formulations, okay? We have enough problems just dealing with conventional tobacco products in data review, let alone everything else out there.

So I'm going to say to the question is basically what we know about the toxicology or the flavors that are out there -- and this stuff is in the literature, folks. Inhalation experiments, toxicology is out there, for glycerol, for PG, for these flavors. It's in the literature, okay? Go read it.

I'm going to come here, and I say based on what's out there in the literature and what I know and what I've seen over my career is, is there -- is likely a product space includes products that have much lower hazards than especially conventional cigarettes, and some of the larger e-cigarettes, and have good consumer acceptance.

We have this product space. Can we work by voluntary consensus standards dealing with the standard on product composition, a standard on product testing and standard test methods? This is all consensus standards. You know, we can -- we have -- already have an ISO tobacco committee working as a TAG under ANSI. We have all these other organizations. I've certainly worked in the past with ASTM committees. Let's get these -- try to work together, product standards, performance standards, and test methods, okay? So we get all the interested parties, producers, users, consumers, general interests, sit down under the auspices of one of these standards-generated organizations, and come down to an approach which defines acceptable components for an e-liquid compound and concentrations, and device standards, and test standards and test methods. That's one approach. Voluntary consensus standards.

Another approach is -- remember here, we have a lot of over-the-counter pharmaceuticals. These are things, you know, this includes the OTC monographs, even includes warning labels. Like you look for some of the cold preparations, do not take with alcohol, do not take when you're taking other medications. Can we use the same approach that's used for cold tablets, certain bronchodilators, whatever, as a way of putting -- having in a simpler regulatory system for e-liquids and e-cigarettes? In other words, what's allowed, what's not allowed? This is an example here, okay, of things that I thought about that, hey, what I'd allow with the appropriate purity certificates analysis, et—cetera. There are certain things I would not allow in an e-liquid I found already at my work. I'd allow certain volatile flavors, lots of things of known composition at the MULs appropriate based on the toxicology. I would not allow nonvolatile flavors that are going to pyrolyze on the nichrome wire, mixtures of varying composition, thermally unstable mixtures, and obviously, we have the strong allergens and the cytotoxic agents.

So what we're basically saying here is e-liquids and product space would not require extensive testing. Just make sure we're using the right grade of materials and have our

certificates of analysis and a way of verifying those certificates of analysis by occasional checking the analytical.

So, anyway, take-home messages. We have this class of products that we have done human biomarkering on them, the toxicology, the chemistry that basically show a very low degree of hazard versus to both users and bystanders, okay? Thus, we don't need the extensive testing if we basically can run this thing as we run an OTC monograph-type thing for an over-the-counter pharmaceutical or by consensus standards. The extensive testing goes in for people that want to bring in novel products that are not part of the product space that we want to go for initially. Yeah, if someone wants to bring other things, let's -- then they have to show that they are truly no more hazardous than what we've already defined in product space.

And also, finally here, is a lot of the hazardous, potentially hazardous constituent testing that's labeled for conventional tobacco products isn't appropriate for e-cigarettes. Let's face it. We have no carbon monoxide, no nitrogen oxides, no hydrogen cyanides, no aromatic amides, et cetera.

So thank you very much.

(Applause.)

DR. DRESLER: Okay. Our next presenter, and I know your program says that it has two speakers, but Dr. Colburn will be doing both. And he'll be speaking on Voluntary Standards, Mandatory Standards, and Special Controls: Considerations for Performance Standards Development.

Dr. Colburn from CDRH, Centers for -- I should read it, yeah -- Center for Devices and Radiologic Health. Sorry about that.

MR. COLBURN: Thank you.

Good morning. And before I start, I guess I need to give a few disclosures, but, one, I'm not Carol Herman. She sends her apologies. She fell ill, and due to her work, she travels quite extensively, and I think she caught a bug somewhere along between China and Europe and New Orleans, or somewhere else. So I send her apologies. But I did agree to kind of present her slides to the group as an example of a standard developing organization.

A second disclosure. I'm actually not a Ph.D. I'm a nurse, a master's-prepared nurse. I do appreciate the accolade, and I just couldn't bear the thought of going to

school that extra couple years, I guess. So my apologies for that.

Third, I will be presenting my talk from the focus of how the FDA Center for Devices and Radiological Health utilized the voluntary consensus standards and its regulatory science and its approaches. I'm not here to be promoting or discussing or even suggesting how the Center for Tobacco Products should consider the use of these, but it is -- I was asked to come and describe a methodology that some of the centers, and specifically Center for Devices, does utilize voluntary consensus standards and how that was given birth to form the overall National Transfer Technology Advancement Act and the OMB Circular A-119, which kind of provides the guidelines to the agencies on how they could participate and utilize standards. And I think John touched on some of that in his 12th slide, a little bit about, you know, some of the desires and how consensus standards can be beneficial.

So with that, I will try to go through a little bit on Carol's slides, and then I'll give a brief overview of how the Center for Devices program works in this space. We have a very robust program. And AAMI is one of several organizations that we are a member of. So I will try to go through with

this, and -- is that right one? Yes. All right. Got my buttons. They left it nice and easy. So I would say this little device here complies with HE75, which is a usability standard. It has three buttons on it. It's very simple for someone like myself, who -- I guess you thought I was a Ph.D., but because of these nice devices, I can look smart and make them work for you, so thank God.

All right. So who is AAMI? AAMI is an accredited standard developing organization underneath the American National Standards Association, or Institute, and they have more than 7,000 members. And just from a show of hands, other than I know my FDA person, who here has a membership to a standard developing organization? One, two, three, four, five, six. So a lot of this is going to seem like alphabet soup to you. Just like your previous discussions in the area of Center of Tobacco was alphabet soup to me, where I didn't understand, you're going to get your share of alphabet soup here from a different area if you're not familiar with standards. But I hope at the end of this, you might understand what a voluntary consensus standards organization is and how a federal agency, such as FDA, does have memberships into these organizations.

As it shows up there, there's over 300 different corporate institutional members. We are a sustaining member within this organization. We do sit on their board of directors. We are involved with their foundation. And we sit on virtually every one of their working groups. Same as with other organizations like CLSI, ASTM, a number of others. I think we're currently just in the Center for Devices on about 26 different standard-developing organizations because we find very, very strong ties and for us to be able to get our work through them.

As mentioned, they are an accredited association. ANSI is, if you kind of do an analogy to maybe hospital accreditations, ANSI is to AAMI as JCAHO is to a hospital. They do the accreditation. It's not mandatory that the organizations are accredited, but there is great worth in that accreditation process. It allows the federal government to have an understanding of how standards are developed through these organizations going through the criteria and the essential requirements. So there is great value and understanding that it is an accredited organization.

They administer several technical committees within the international space, such as ISO and IEC. They hold both a U.S. TAG and secretariat to several of those, which we'll see

examples from. So it is one of our -- organizations like AAMI and ASTM and others, through the accreditation of ANSI, allows us to get involved with the international standards, which, of course, from a globalization and marketing and making sure that the U.S. marketplace is strong, is a very important tool for us. And as a federal agency, we want to do what we can to make sure the U.S. marketplace is strong through these types of organizations.

Standards, obviously -- and this is one of their main scopes -- standards should only be developed only when there is a clear need. And that's very simple. So if I was speaking on behalf of Carol Herman, why would I want to build a standard for you that I'm not going to be able to sell and at least sustain the cost that it took to build that standard, right? So they definitely look at the scope when these newer kind of proposals come in. And they want to make sure that these standards are something that is a true need to whatever the scope for that standard that is driving for.

"One product, one standard, one test worldwide." A couple of years ago, I gave a talk on something called standards wars, and that was because we do see times where there might be three or four different organizations working on standards

in a similar space. And, you know, for all of us that are members to that, that just means we're working four times as hard with four times as much time, and we would like to have that done in one single place with all the right experts there. And so that's the goal of the standard developing organizations. And it is through the ability of members who can be involved in a number of different organizations to help oversee that type of activity.

That button didn't work that time. Different types of documents that AAMI does produce. They do basic performance and safety standards. Those can be recommendations on labeling, basic safety and performance criteria primarily for the device manufacturers. We do utilize them in our -- in the Center for Devices and rec what we do -- we call -- we recognize them through the authority that we have in our act. And that does help us communicate both to our staff internally and educate, as well as to the industry members submitting documents in on how they went through and demonstrated some level of maybe safety and effectiveness, or they addressed a certain process through risk management, and the number of different aspects that standards do address.

AAMI also has what's called recommended practices. These

are guidelines for use, care, evaluation, typically for the end user. So maybe the people that do the disinfection of products in the hospital, they write guidelines so people would understand how the design of a particular device, and maybe it's through its labeling on the recommendations that it goes through, a rigorous protocol is utilized. So a recommended practice is created for that. It's not a best practice. It's a recommended practice. A little bit different.

We also have technical information reports, which kind of get a little bit more into the granularity from some of these massive standards, such as like, say, sterilization, where you need a technical report to get a little bit more understanding. These are similar to the technical specification reports that you might find in an ISO or IEC standard.

This is just a big kind of snapshot of some of the areas in ISO and IEC that AAMI is involved in, so they obviously -- and I think if my numbers are remembered correct, about 70% of their work is actually through the ISO and IEC portals. So although they're a U.S. national standards developing organization, 70% of their work is to make sure they're

involved in there. And that's because their stakeholders are, by and large, global marketers. You know, medical devices are typically the same here as they are in China or as they are in Europe or anywhere else. And I'm referring to the user end of it, maybe not the manufacturing end. But the reason why the international standards are so important is that people want to be able to manufacture their stuff globally. So an international standard in this case is more appropriate for this type of manufacturing company.

Who can participate in standards development? Any stakeholder who has an interest essentially. We have an interest, we're a member, manufacturers, academia, users, consumer advocates, et cetera.

And who writes standards? These are the technical committees, the subject matter experts that are part of these organizations. It's led through a leadership of co-chairs, one producer and one general interest or user representative generally in the AAMI model, which helps balance out some of the issues. The goal and overarching endpoint is to make sure whatever that standard represents didn't get overshadowed by a majority that didn't represent the balance of what needs to come into the standard developing process.

Quick flowcharts. Again, we're going to start getting you into charts and alphabet soup here. You go through a proposal into the drafting stages, balloting. You get the public review. Even if you're not a member, as an accreditation, one of the processes through ANSI, all standards go up through something called standards action so the general public has the opportunity to submit comments. And that is a very common thing to see especially when we're addressing safety issues, where the public is well aware of a safety issue going on in the field. And so we do receive comments. And it is the responsibility of the organization to make sure those comments are heard by the committee and that the person who did submit those comments understands that all those comments were received, and if they were accepted or not. Goes through an approval process and then to publication. And then at that point, it is there for the stakeholders, the Agency can look at those standards and decide how they would want to utilize them, and I'll describe those later.

So it goes through all the different stages. And I'm not going to hit on all these, but I kind of just discussed them earlier. But one of the things I want to impress upon -- you'll see this slide twice, so I'm going to say Carol stole

this slide, but you'll see it a little bit larger later. But what it really exemplifies is that being involved early is the most important way to ensure that if you have something to say, that it gets heard and that it has a chance to be incorporated in a more granular and more technical sense. If you come in towards the latter stages of the development of a standard, it's very hard to wiggle that in because the standard has already been set from a technical aspect. So it's very important to be involved and not go in at the end and say I don't like it. Well, you know, you're going to have to wait till the next cycle. So the impression is, you know, try to be involved at an early stage. You're seen as a valuable expert, and we want to hear that expertise at the most earliest stage possible.

Communicants. There's a balloting stage, obviously, that it goes through. Each organization has a formal test or consensus, you know, through this ANSI accreditation process. And as I mentioned earlier, there is a formal process required to ensure the openness and due process through that open public review. And that's real important. And I'll describe a little bit later on how our centers approached utilizing standards and our authorities and how that kind of matches a

little bit about our good guidance practices and how we develop guidance and the requirements that we see and the similarities of getting public comment before going out to something final, very similar into the approach of how a standard is developed, which is why we have really found the value of being involved in that, because we do get to hear from the stakeholders who would otherwise comment into a guidance. And we're finding that we can get more into standards sometimes. And I'm seeing smiles from some of our technical experts in the room.

Individuals cannot comment directly on ISO or IEC documents but must work through their national member body or national committee. And that's real important to understand that as a member to any ISO committee, you're not there on your own behalf, but you're there on part of the U.S. delegation. So I myself, you know, sit on several international committees, but I'm not there representing FDA. I'm representing the U.S. delegation. And so the U.S. is the body that we work through. Those are held through and managed through ANSI. And so you need to make sure you're submitting your comments to the appropriate person when working into an international standard. And John did mention that there is an

ISO committee that deals with tobacco products. And so if you wanted to comment onto those, you would have to make sure you understand who the appropriate organization here is in the U.S. that holds that U.S. TAG.

All right. I'm going to go through. Obviously, because there's a process, a due process and a balance, there is even an ability to appeal a final approval. We have found in certain standards that maybe even through the whole stage of commenting and balloting and, you know, it makes it through and gets published, and we find out, oh, jeez, look, that standard really still has potential to even create a public health risk if it was going to be adopted, referenced, or just utilized in any manner which a standard could be. There is a formal process where you can request for an appeal of a standard, and that's to ensure those type of issues do take place. Standards are developed by experts. Experts are humans. Humans err. So we do realize you need to have a built-in check kind of for those types of processes as well.

Which organization is the best author for a document? That's always an interesting slide. But it really, you know, each organization, and AAMI is one example, where they have a specific scope and a specific concentration on areas. A lot

of those areas do overarch some of the discussions that we had today. There is committees on biocompatibility. There's committees on battery safety, risk management, quality systems, things like that. But it is focused at medical devices. An area for e-cigarettes would have to consider if they wanted to develop standards; if there was an already existing committee, what would be the appropriate organization for such standards to take place, or are there current existing standards so that we don't have to reinvent the wheel that we could utilize and adopt for this process?

And I'm just going to continue to go through here so I can get through our comments. Let's see. All right. So this is just a quick analogy showing the, you know, the stages that you would see in the standard-developing process. So AAMI has, you know, new work item proposals, IEC has a new proposal, and new work item proposal is similar in ISO, and it goes through the different stages to the final drafts. And from there, the publication of a document is made. You'll see that it is very similar -- and if you heard what I mentioned earlier, the medical device industry is largely a global industry, and so their standards are largely in that global platform. You see one organization here that is focused in

the medical device arena really tried to match itself to ensure that it's doing the best for its stakeholders and its members.

So with that, I will continue on into my presentation, and then later, I think we'll have time for a little panel, and I'll be happy to take any questions that we have.

Okay. Let's see -- oh, do you guys do the next slide, or do I just keep going?

(Laughter.)

MR. COLBURN: I was too fast for you. All right. So a bunch more slides, bunch more alphabet soup from a Center for Devices perspective here. So as mentioned, I am the Director of CDRH's Standards Program, the Center for Devices and Radiological Health. And later you'll actually hear from one of our experts. I don't propose -- my last disclaimer is I'm not an expert in anything. That's why they made me the director of the program. I have about 375 experts that operate in the over 600 different working groups that the Center for Devices and Radiological Health operates within. And that's because we have products and devices of all different types, shapes, sizes, processes needing different performance requirements, and it's just a huge myriad of areas

that we need to be involved in. So, by golly, they wouldn't have me be involved in. They just say you're the director, and let everyone else do the hard work for you.

All right. So I'm going to kind of give you a perspective of, you know, where did this all start, why is the FDA so involved. I mentioned 375 people, 600 different working groups, in a little teeny Center of Devices and Radiological Health that has about, you know, it just -- one of the smaller centers here, actually, in the Agency. And by God, it actually represents over 10% of the government's involvement in standards. And that's because of the types of products and the wide variance of them. But there is a precipitous factor of where this all drives from.

And so I'm going to go through, and you'll see some of this up there, but NIST is the National Institute of Standards and Technology underneath the Department of Commerce. And they've been assigned the responsibility to coordinate the federal, state, and local technical standards and performing assessment activities, as well as coordinate those in the private sector. And they help manage the commerce standards through a committee called the Interagency Committee on Standards Policy, which I actually am a member to, and so a

number of different organizations like the FCC, OSHA, and Department of Labor, the CPSC, EPA. And this is a group of government members that work together to try to make sure they understand what the roles and responsibilities of their departments or agencies are to make sure we're meeting the needs of what the direction NIST has, because they have an act that directs them to help federal agencies to adopt private sector standards in lieu of creating government-unique non-consensus standards.

It also tells them to encourage participation in these standards bodies. One such that we've seen is AAMI, as we saw before. We've also made mention of ASTM and a number of others. It does direct NIST to coordinate the federal, state, and local governments to have greater reliance on using voluntary standards and decrease dependency on in-house standards. And, truly, the reason why that is is it's a cost factor. It is very, very laborious and costly to develop your own government-unique standard. The government realizes that, stakeholders realize that. So this is a way for us to help understand what's another tool that we can use to help meet our needs, and is that tool more effective.

The OMB circular is another document that came out to help

set forth the requirements for making sure the Agency understands that, yes, it is okay for you to sit at the table and discuss your needs as a stakeholder in this process. But we do want to hear -- the office of the White House does want to hear what your involvement is. How are you utilizing voluntary consensus standards? Where are your needs where you're developing government-unique standards? Because it's not prohibited, obviously, to write a government-unique standard, but they do want to collect that type of information so they understand where are government-unique standards still needed and why, and there is a way that we can help develop other processes to help reduce cost from the -- to the government by developing different processes to where standards or other processes would exist. And that's part of the tool of what this circular does. It also discusses the incorporation by reference and where standards come in.

And I see my yellow light coming on. I'm going to get moving. So as I discussed, it eliminates unnecessary cost. It promotes the economic competition by getting the stakeholders when you're at the table. And we find great value in hearing from our stakeholders. In fact, just yesterday, we had a phenomenal meeting downtown with a

standard-developing organization. We got a lot of great feedback and support because we were able to be there and discuss the regulatory science needs and a very technical standard dealing with biological gas pathways of breathing circuits. I mean, that's a very technical standard. I'm not even going to begin to tell you what it's about. But because we were able to be there, all the other stakeholders felt that it was a very useful tool for them.

We do have our own guidelines that tell us how to participate and why, you know, why we want the encouragement on participation, give some direction to the experts about how we should be doing this. None of it's a secret. We have our own policy. We have our own staff manual guide that sets policies for each center and the development on the use of standards and common definitions. And I do have on the website there where you can find those things.

For our own program, we have our own authorities written into the Medical Device Amendments Act, and it was brought out where that's where we started writing our own government-unique standards. It was very difficult obviously to keep up with all the different technologies, so we had the Modernization Act, which brought in and asked us to formally

recognize, all or in part, a standard through a declaration of conformity. And this allows us to, you know, to communicate to the public those voluntary consensus standards which we feel are very valuable to us, and we would encourage the industry stakeholders to communicate to us on how they did utilize that. And we find that it's a very good dialogue and understanding of how they went through the technical aspects.

So I'm still okay. Make me sweat, and then you give me green. Is what I'm saying good maybe? Okay.

So real quick, I'm not going to read this word for word for you, but this is, in fact, what's written into our Food and Drug, the Modernization Act. But it just says, you know, the Agency, by publication in the *Federal Register*, can recognize all or part of a standard where a person may submit a declaration of conformity. And if they elect to use that standard, they would provide that declaration of conformity to the Agency that certifies that the device is in conformance with such standard. It says that they are in conformance, not that they will be, not that they'll think about it, but they are in conformance. And there are penalties to lying to the government when you do go through that formal declaration process.

We also have the authority written into this to withdraw such a standard. I did mention where standards maybe are, you know, we thought they were great, we recognized them, and then maybe we learned through the stakeholders or through an appeals process that that standard maybe didn't quite hit the mark where we really wanted. And so we do have the authority to withdraw a standard. Or maybe a standard has been updated, the new and improved version. Newer technology keeps moving along in our field, so we can recognize a newer standard as well. And that communication tool that we do through the *Federal Register* Notice, and then we have a website that -- a database that shows all the standards that we recognize, is a really great tool both to educate our own staff, but as well as the stakeholders who need to come through our regulatory processes to understand what is the Agency's view on if you would choose to use this voluntary consensus standard approach.

This kind of just goes into a little bit about the -- you know, a little bit further about if we accept the declaration of conformity. Some standards, and not very many, but some standards do have a complete quantitative approach to them. They have endpoints built into them. The test methods are

very specific. And a company may be able to just say we declare a conformance to that standard. And the Agency might say thank you. But many standards, and I would say 70 to 80% of them, aren't that specific. They do have ranges or maybe a minimum, but they don't have everything. And so we may still need a summary test report in support of a declaration where someone would choose to use that standard. And if we agreed to all the endpoints and how they justified why those endpoints did mitigate any risks through a risk assessment and the channel of other standards, then we would again say thank you, or we might ask for some additional information.

One thing I always tell people is that -- and this helps relax both the Agency personnel that get, you know, a little squirmish when we say, you know, we're going to recognize this standard, but also as a conformative tool to the end users, that conformance is not your clearance to the market; conformance doesn't give you approval. The way to get to the market is a big puzzle, right? And there's a lot of pieces. And standards might give you a few of those pieces to help give you that picture. The more standards that are utilized and communicated between the FDA Center for Devices and Radiological Health and its stakeholders, more of that picture

gets filled in, and it does help us get devices to market. It helps us track how those standards are effective tools for that. But it is always important to make sure that they don't feel that I use that standard, therefore I get to go to market. That's not the case. There's always much more to getting somewhere.

There is an important tool to always remember that falsifying anything in your application is against the law. And so we do have that authority in here that describes that. Any device for which a declaration of conformity has been falsified is adulterated. So if you're going to conform, you need to conform, and you must conform. If an inspector found out you didn't, you are now adulterated.

So real quick, just to finish off here, then, you know, the center here uses -- and the Agency, by and large, uses regulations and product standards as the yardsticks that define the specific requirements manufacturers can follow to assure product safety and provide accurate information to help professional consumers. All in one breath. But they are important because they do build consistency, credibility. They hit all these different areas, from performance to characteristics down to labeling and risk assessments. They

give greater potential to save time and money for the Agency. They open participation by all affected parties. They minimize or eliminate inconsistent standards internationally and can lead to national or international harmonization if that product would require such. In fact, just today, we've had presenters from Italy, Germany, the U.K., the U.S., and I think several others. So it's obviously something that needs to be considered in this space as well, which is why we already have one committee in ISO.

Standards often do represent leading-edge thinking on an issue. It may not be the tip of the spear, but what it does is it gets the majority up to a level where safety can be addressed, and then we have a better understanding of how to take that next step moving forward to address a safety concern if we understand where the bar is set through other standards that are developed.

The last few slides, and I know I'm running real close on time here, just really talks about the government's participation standard. And so maybe this is my message to my other colleagues in the government of why it is important to consider being a participant in the standards development process. And it's not that you are the technical expert, but

you are -- the government is usually the only one who sits at the table that truly understands their regulatory responsibilities, their regulatory laws, and it is very helpful for the other stakeholders to have that understanding as part of the balance. And that makes the standard a much more effective tool. And that's one of the messages that I always stand and give when we talk about government's participation. And that's really where I'd like to end, is why it's so important.

Here's that slide again, obviously important. The earlier that we're involved, the more effective our tool of bringing regulatory science into a standard is there, and it is a very important thing for us when we are able to be there.

So, bottom line, participation is key. To influence outcomes, you need to be involved. You need to be there. These are wonderful venues to do these types of activities to figure out what are our next steps, what can we do to collaborate. So I do appreciate and want to thank the Center for Tobacco Products to invite us to have this discussion, and all the stakeholders that presented earlier. I think your comments really hit a lot of areas that standards probably will be listening to and waiting for your new work item

proposals in the future.

So with that, I leave you with an example of about 100 or so different standards that we threw into the periodic table that we recognize over at the Center for Devices and Radiological Health.

Thank you.

(Applause.)

DR. DRESLER: I did exercise moderator's prerogative since he had to give somebody else's slides. And if you all have done that, he got an extra few minutes. So thank you very much for doing that.

Okay. Our next speaker, Sud Patwardhan, from Nicoventures, British American Tobacco Group, will be speaking on -- I screwed up. I got so excited by my moderator's prerogative. I'm sorry.

Ken Skodacek is going to be speaking on Standards Considerations for Battery-Powered Devices. And he is from the FDA Center for Devices and Radiological Health.

Ken, I'm very sorry. You're up next.

MR. SKODACEK: Good morning. So I'm here today to present to you the Standards Considerations for Battery-Powered Devices. I'm actually the Co-Leader of the Center's Battery-

Powered Medical Devices Working Group. I work in the Office of Device Evaluation as a policy analyst and have been with FDA for 6 years before coming from the medical device industry.

As disclosures, I'm an FDA employee and have no relationship or financial interests to disclose.

So you're probably thinking why does FDA care about batteries and battery-powered devices. So it's all about safety and performance. And you're going to see that throughout my presentations today.

So FDA does not regulate batteries, but FDA does regulate medical devices, and batteries are one of the critical components in those devices. Failure of battery can result in catastrophic consequences and failures of the medical device.

As an electrical engineer, I know that a power source as a battery can be simplified and presented using this annotation here. A battery seems like such a simple thing. In fact, it's a very complex component. The available voltage and current vary depending on the design or the manufacturing characteristics, the load, the temperature, the storage time, and for rechargeable batteries, the number and depth of discharge and recharge cycles. Batteries are anything but

simple.

Earlier today and throughout this workshop, I've seen a lot of presentations about how the devices are performing, and I'm wondering if they're using a standard battery, if they're using a power supply, how they're regulating and making sure that that battery has the same operating characteristics through all the testing, because independent of all the other characteristics of the e-liquids and the components themselves, the battery itself can affect the performance of that product.

The table here summarizes some of the common problems with batteries independent of the medical device. As you can see here, these problems can be very serious, including overheating, fires, and explosions. And I'm sure you can all agree that no one wants any of those in e-cigarettes.

So what could possibly go wrong with a battery-powered medical device? So now let's look at some of the -- beyond the battery itself and look at some of the examples of problems with medical devices caused by battery-related issues.

So this is an automated external defibrillator, or AED. This is a recent story here from the local news in the

Washington, D.C. metro area. A passenger died after suffering a sudden cardiac arrest when the AED could not be used because the battery was depleted. In fact, an analysis of FDA's database identified that approximately 5% of all reports and adverse events during a 3½-year period were related to battery. That's 75,000 events. In fact, battery-related issues are one of the leading causes of device malfunctions of a variety of critical devices, such as external defibrillators, infusion pumps, and ventilators.

Now, you're probably thinking that batteries are important especially in a life-saving device like an AED, but what could possibly go wrong with low-risk devices? So here I present to you an electronic thermometer. How many of you have used an electronic thermometer before or have children? So I'm a recent new parent, and I have a 4-month-old son at home. I left him this morning. And I can imagine all the challenges that I'm going to have in the years ahead. But one of the things that I know is that my son, luckily, has not been sick yet. But I do recall when the physician told me that their temperature has to get above a certain level -- or if it's below a certain level, if it's okay, if it's above a certain level, you should immediately rush to the hospital. So you

can imagine that we bought a very high-quality electronic thermometer. Now I want you to imagine that that electronic thermometer actually isn't so accurate as the battery voltage decreases. In some cases, we found that the electronic thermometers don't present the accurate temperature as the battery is nearly depleted, and it might not be presented to the end user.

Another example of a medical device, electronic toothbrush or an electric toothbrush. So you probably use your electric toothbrush two to three times a day. And you're probably thinking what could possibly go wrong with my electric toothbrush? What, it shuts off early or it doesn't work? Well, you can imagine brushing your teeth in the morning, and all of the sudden, bang, you hear an explosion, your ears are ringing, and you're trying to figure out what's going on. This, in fact, happened. In some cases, electronic toothbrushes were exploding as a result of the gases that were being emitted from the battery, which were sealed inside the plastic case. So that plastic case is sealed to prevent water getting in, but in some cases, that mechanism prevents the explosive gases from getting out.

Another example for you. So a sinus irrigation system.

So say you have a sinus infection or you had some sinus surgery and you're trying to prevent an infection. And you basically use this to wash saline through your sinus passages. Now, have you ever opened a remote that hasn't been used for a while, say, for your TV, and you open it up, it's not working, and what do you see in there? You see the batteries are corroded. Now, can you imagine if the design of the device was such that the battery corrosion in those materials leaked into the saline, and then you were rinsing those materials through your sinus cavities? No one wants that.

So in order to proactively address these and many other issues, the FDA formed what's called the Battery Working Group. Our mission and objectives are provided here on this slide. The group includes staff from various parts of the organization: the Office of Device Evaluation, Office of Science and Engineering Labs, Office of Surveillance and Biometrics, and Office of Communication and Education.

Last summer, we hosted a two-day workshop much like today's workshop. The goals of the workshop are listed here. We had nearly 700 individuals registered for the workshop, including representatives from the medical device manufacturers, battery manufacturers, battery testing firms,

healthcare providers, patients, as well as U.S. and international regulators. In the pre-meeting survey, nearly one-third of those registered with the workshop identified their goal as to learn FDA's expectations and requirements for regulation of batteries. However, we brought everyone together to learn as much as we could about what to do in the future.

FDA currently recognizes three standards for batteries: UL 1642 for lithium batteries, which are commonly used in many consumer products; UL 2054 for household and commercial batteries; and IEC 62133, which is focused on the safety requirements for secondary batteries.

So to put these standards in context, standards can be highly technical documents that are negotiated and agreed upon by tenured technical experts. However, I'd like you to understand some of the content of the document. Here, you can see that it's important that the battery doesn't explode or catch fire.

So is the issue with the battery or the battery-powered device? The answer is both. In order to emphasize this point, I would like to share a quote from one of my colleagues, Hamed Ghods: "If it is impossible to assure that

the battery failure cannot be prevented, the system can often be designed such that the failure cannot harm the patient."

So here are two examples of standards that are referenced quite frequently for electronic medical devices. The first standard applies to basic safety and essential performance, and the second standard applies to electromagnetic compatibility or interference. So you can picture someone using an electronic cigarette while they're holding their smartphone to their head. And you can imagine maybe today that smartphone doesn't interfere with the cigarette, but as electronic cigarettes become more complex, there could be interference and inappropriate performance.

So IEC 60601-1 is over 300 pages long. But I'd like to provide an example of a standard that might be relevant to the products that we're discussing today. So they showed that over time that the temperature of the parts of the device that are in contact with the user or patient maintains a certain level. So, obviously, you wouldn't want the electronic cigarette getting overly hot while it's being used, just like your smartphone gets warm when you're using it.

As you can imagine, there are standards for all kinds of consumer products, including mobile phones, laptops, and

children's toys. Coincidentally, the Consumer Product Safety Commission set out a notice to consumers just one day before the FDA workshop on battery-powered medical devices reminding users about shopping safely when purchasing batteries and chargers for use with their smartphones. That notice also reminded everyone that there are standards to improve the safety and performance of these devices.

So how is this discussion about standards relevant to e-cigarettes? Well, here's a recent story. We've seen many similar stories in this, and my colleagues and friends from across the nation are always sending me stories about exploding batteries. And I think it's easy to agree that we don't want to have things happen. Coincidentally, I think the rest of this article, if you actually read this one from the CBS News, has a statement from a manufacturer that says they've never heard of this problem before. So I think it's hard to believe now with all these events.

So what are some concerns? So these concerns shouldn't be a surprise for anyone here today. In fact, I found a list of concerns online. And one of the speakers mentioned clone devices, so there's a lot of copycat devices. And, of course, if you're copycatting the battery of the device itself, those

are just as subject to failure.

And as I conclude my presentation, I suggest that you consider this question. How would standards improve the safety and performance of e-cigarettes?

Thanks for attending today's workshop, and for the Center for Tobacco Products for having me speak. Thank you.

(Applause.)

DR. DRESLER: Okay. Now for Sud Patwardhan from Nicoventures, British American Tobacco Group, speaking on E-cigarette Regulation in the European Union: Progress Made on Product Quality and Safety Standards.

DR. PATWARDHAN: Hello, all. I'm Sud, or Sudhanshu, Patwardhan for short. I work at Nicoventures, which is part of British American Tobacco Group, and I've trained as a medical doctor back in India, have worked in the BAT Group for the last 9 years in the Tobacco Harm Reduction Program of the company, and for the last 2 years in Nicoventures, which is part of BAT, specifically looking at regulation, the regulatory landscape and specifically focused on electronic cigarettes.

I want to thank the FDA CTP for the opportunity for us to bring the European perspective, in terms of regulation, how

things are changing there, what's law, and also activities in the standards space that are happening at a very rapid pace in the EU.

So on that note, just give a bit of -- oh, is it on one -- an outline of what I'm going to talk about. Just brief introduction about Nicoventures, Tobacco Product Directive, and what it means and where it is at the moment, and the standards activities. There's a lot of acronyms in this presentation, and so if you find it a bit too overwhelming or if you doze off, what I would like you to remember or take away from this presentation is this, that the TPD or the Tobacco Product Directive is law now. It came into force earlier this year in the EU, in the European Union, and it's got a timeframe of, over the next 2 to 3 years, for it to be ruled out and implemented in the member states of the European Union. So that's one thing to bear in mind. And the second message to take home from this, I would like, is that standards initiatives in the U.K. and France, particularly on product quality and product safety, are well underway and in a very constructive, positive, multi-stakeholder sort of process that's allowing it to really take in a lot of views from different sectors, different stakeholders, and hoping to

really raise quality and safety standards to assure consumers and regulators alike. So that is the messages. Now back to the presentation obviously.

Nicoventures is part of the BAT Group, as I said earlier. It's separate from the tobacco business. Our focus is the development and production of innovative, high-quality inhaled nicotine products that meet relevant regulatory requirements. Our aim is to provide adult smokers -- the emphasis is very clear -- adult smokers and users of nicotine products who want to reduce or completely replace their smoking habit with less risky alternatives and which are acceptable to them as alternatives. And that's what Nicoventures stands for. We have products in the U.K. market, electronic cigarette products.

Now, on to TPD. The Tobacco Product Directive, it lays down the rules governing the manufacture, the presentation, the sale of tobacco and related products in the European Union. It's sort of a umbrella regulatory framework for all European member states in the European Union obviously. That's 28 of those member states, an example being the U.K., France, Germany, Portugal, Spain, and so on and so forth. So the TPD is that overarching framework. So since it was

revised this year, it now also includes electronic cigarettes, but of course, it covers tobacco products, such as cigarettes, roll your own tobacco, smokeless tobacco, herbal products for smoking, and so on.

The new TPD, which is TPD2, some people call it, came into force earlier this year in May, and the member states are obliged to transpose that, so put into their local and national regulations in the next 2 -- over the next 2 years with another 6 months to a year for actual implementation and enforcement. So that's the timeline. The TPD is comprised of 33 articles of which the article of interest for us in this audience for today's presentation is Article 20, which focuses on electronic cigarettes.

So what does the TPD do for electronic cigarettes? What it does, given the way it is designed, is it provides two options for member states and for manufacturers in member states. The TPD option for e-cigarettes is where, as long as the products, the e-cigarettes are within limit, in terms of the nicotine content, in this case 20 mg/mL, or the volume of the refill containers not more than 10 mL, or the volume of the tank or the cartridge not to exceed 2 mL, it can fall under the TPD part of e-cigarettes, or e-cigarettes can be

part of TPD in that sense. Of course, with that come restrictions on what can and cannot be said. And, of course, you can't make therapeutic claims, there'll be health warnings mandated by the TPD itself and also by the state, member state, there'll be requirements for childproofing, and so on and so forth. There'll be a requirement of premarket notification as well, which is now being defined as we speak.

The other option, of course, is for the manufacturer to go the medicines route. So a manufacturer could put the product to the medicines agency of that country and say, listen, we would like to have a marketing authorization for this product for smoking cessation. And that would give them a certain different range of freedoms in terms of distribution depending on which country you were in, of course. So, for example, in the U.K., you would be able to sell an NRT product for cessation not only on prescription or over-the-counter, but also in general sales in a convenience store, for example. That may not be true for other European markets, mind you, but the range of freedoms, the ability to make -- exist with that route.

So what happens in the TPD next? As I mentioned earlier, that it is law, as published in the official journal of the

European Union in May earlier this year. Now, in the next 2 years, the Commission, which is the European Commission sitting in Brussels, will be defining elements of what needs to go or the template that's required for submitting data for premarket notification by manufacturers. The bottom line of all that, the left-hand slide of this slide is essentially the Commission is working on it now. It's in a consultation mode. It's developing that template, and that will be out in the next year or so.

At the same time, the member states, the U.K., Germany, France, are also working on how to define certain specific bits of the TPD that they are required to do in terms of transposition or translating the TPD into actually implementing actual law for their national regulations. And that includes specific content on health warnings, advertising, or advertising restrictions in some cases, and some more nitty-gritty on the cross-border sales and elements of the TPD that are not yet completely defined. So this is all happening.

Now, this is where I'm going to transition into what does that mean for consumers, for the regulatory landscape going forward, and for public health, and for the industry, of

course. So I'm just going to take a pause here, because what it means is products, e-cigarettes in the European Union, most markets can continue to be there till 2016 or a bit later than that the way they are at the moment. All the requirements mentioned on the left-hand column under Article 20 will not really come into force in most markets for a while to come. Now, let's keep that thought, hold that thought.

The other thing is you might see data coming from the U.K., for example, which excites a lot of public health advocates, those who believe in tobacco harm reduction, looking at two million smokers who have either completely or partially switched out of smoking -- cigarettes. And indeed it is a massive public health story there. The missed opportunity there and the potential positive opportunity there is that the remaining eight million smokers in the U.K. are either ones who have not tried e-cigarettes at all or are a bit hesitant to try e-cigarettes given the news and the media or their personal experiences in terms of quality and safety of products.

So there is a need here, and there is this sort of regulatory vacuum, if I can use that phrase, for the next 2 years, where if the industry takes leadership and takes

along regulators and other key stakeholders with them in the U.K. and elsewhere in the EU, they have an opportunity to raise -- voluntarily raise product quality and safety standards, and hopefully, it will have a net positive public health impact.

So what's happening in that space then? I'll talk about BSI, the British Standards Institution, and also touch upon AFNOR, which is in France, the French national standards body, and the European-level standards body, which is CEN.

So the BSI commissioned -- so BSI is the U.K. standards body, national standards body, and it's involved as -- probably some of you who are familiar with BSI -- involved in all sorts of standards across all sorts of industries, including heavy engineering, hardware, software and services, and so on and so forth. For them, they saw the opportunity and the need for a standard in the electronic cigarette space. They approached the E-Cigarette Trade Association in the U.K., ECTA, earlier this year to say can we put something together as a industry-sponsored standard, which -- what we call as a industry best practice but effectively is going to be a publicly available specification that companies can voluntarily choose to sign up to and that allows them to say

that, yes, we are complying with this. Usually, the pathway for such voluntary standards is they can then migrate up to become a national standard and subsequently a European regional standard, potentially an international standard. So this, as far as I know, and as far as I've seen out there so far, the first initiative from a national standards organization to actually go out and say, listen, can we do something about this. There is such a dire need for doing this. And, of course, as you see on the slides, the idea is that this is for manufacturers and for other suppliers in the supply chain and full laboratories who are testing these products to these standards.

So this was initiated. They put a steering group together, which was -- which I believe the intent was to have it as representative as possible, including small, medium, large companies in the e-cigarette business. We were very fortunate as Nicoventures to be invited to be part of that. And we had talked about product standards for the last year and a half. We had put our views out in public conferences, and that is part of the reason we were invited there to that. And we also have public health thought leaders in that steering group, and as well, consumer advocates, actual

consumers of e-cigarettes who are part of the steering group. We also have a trading standards representative. So it is, I believe, a multi-stakeholder sort of process. But then that's to be expected because that's how BSI does their standards anyways.

Now, just a little qualifier here. What I'm putting up here is what is in the draft publicly available specification, or PAS, that was published earlier, in November, which went out for public consultation for 4 weeks, and it elicited an overwhelming response from a wide range of stakeholders. And I believe this was perhaps the largest response BSI ever got on anything in terms of at least nearly 1,000 responses from across different stakeholder groups. And rightly so. I mean, we are all here, and we understand that there's a lot of different views. And the approach that we have taken with the draft PAS, which was published and which elicited that response, was to put the elements of quality standards and safety standards out there in a structured format, perhaps to some people's concern, too much detail for others, maybe not enough there, and of course, there's that review that any consultation will elicit.

So this is just what we have tried to capture in the

draft. Of course, after the consultation, after the responses, we have the next few months to actually go through all those hundreds of responses and try and incorporate some of the very constructive comments into the revised draft. And we still believe that will be -- aiming for publishing it in the first half of 2015. And just to sort of touch upon for the last -- for yesterday's presentations, earlier today, some of the presentations from other companies in the e-cigarette space, everyone is talking about the for product standards. The scientists who are working the space are asking for product standards, and it's like a no-brainer, really. But then the question is, what do you mean by that? What do you put in there? How high do you raise the bar? And what we've tried there is trying to sort of capture some of the key issues that e-cigarettes as a category faced in the minds of public health regulators and consumers.

And we just heard about batteries as a challenge. There are existing directives in the EU where you could easily connect your BSI pass of the draft standard and the published standard subsequently, saying can we follow -- can we recommend that that directive be followed, because that takes care of most of the issues of battery charging and recharging,

as an example. The more contentious ones are, of course, the ones in the field of toxicological risk assessment, and how far do you go in terms of emissions testing? Are there enough testing, validated methods out there can be immediately applied for e-cigarette aerosol that can be then translated into making sense of the data, and so on and so forth.

So there are a lot of things that need to be resolved, but that shouldn't stop us from putting the first draft out there for consultation, which we did, and then the first final product for informing future industry behavior. And if companies start voluntarily complying with this, I think what it achieves is a certain level of confidence in consumers and other stakeholders in the community on what this means and whether they can actually trust the category, because the public health -- the gain is far more than what -- the concerns I raise about. So if you can address some of the easy -- easily addressable concerns, battery charging being one, the quality of ingredients used in the e-liquids, for example, being the other, these are easy ones that can hopefully make the category sustainable long-term and also build up confidence, as I keep on talking about.

So that's that. A reference to what Scott said earlier in

terms of standards wars, thankfully I hope we don't have any standards wars yet. The BSI process is in parallel to the AFNOR process in France, which has a similar sort of similar multi-stakeholder group working on a similar plan. And the good news is that we are talking to them, and between us, we'll be publishing at a sort of similar timeline. And we then also have approached the CEN, which is the European-wide standards body, which also is indicated to be the body that European Commission is going to go for, for actually putting some meat around the existing TPD proposals.

So it looks like it's all sort of in the right direction. And the attempt by some of the industry players to kind of bring together these different ideas and different simple things that can be done to raise the quality and safety standards of products is hopefully getting traction.

And I'm going to leave you with this slide. But the point I'm making is, as I said in the message earlier, that TPD is here, and it's going to be rolled out in terms of implementing and fleshing it out in the next 2½, 3 years. Standards raised by industry in consult with the rest of the key stakeholders and the public health and scientific and regulatory community will hopefully make the category more sustainable. And we're

happy to share these learnings with -- beyond Europe, and hence we are here.

So thanks for your patience, and any questions we'll answer in the panel. Thanks.

(Applause.)

DR. DRESLER: Thank you. And if the panelists can come up to the table, please.

And then I have a question. Is Dr. Quinlan here? Dr. Quinlan for the next panel? We are thinking of doing a little bit of rearranging. I'm not seeing her. Okay. That will alter our ability to do that. And, again, as I'm seeing cards go to the side, that's great. Write your questions on the card and send them to the side, and we'll have the questions come up. And here's what I'm thinking as we're getting this panel going, because we have some extra time, I thought of moving the panel up from right after lunch to right before lunch, but we need the speaker here, Dr. Quinlan. So if she comes in while we're doing this question and this panel, then we might do that. So we'll stay flexible.

Let me move to -- all right. Dr. Lauterbach, this one is for you. What standards are needed for e-cigarettes to assume maximum benefit and minimum risk? That might be a whole panel

question actually, so -- but it does say for Dr. Lauterbach, but I think that's -- we'll start out with that very simple, short question. What standards are needed for e-cigarettes to assure maximum benefit and minimum risk?

DR. LAUTERBACH: Well, part of the process on developing consensus standards is bringing in all concerned parties. I mean, until you bring in producers, users, general interest regulators, you don't have a complete view of what each of the participating parties would like to see in that standard. So this is basically part of the thing of consensus standards is bring in all the concerned parties, and that may modify the result. But I mean, one person would actually have to start off in saying, well, this is putting it out as a draft standard and then seeing where it goes.

DR. DRESLER: Let's have everyone go for that one. If you can turn your microphone off, please, Dr. Lauterbach? Thanks.

MR. COLBURN: So I would agree. I think it's very important, and you know, we did just see some examples of where the European Union and the U.K. are, through BSI, AFNOR, and then it seems like CEN is involved in overseeing. But you know, I guess if we wanted to be a little selfish, we'd be like, well, what about us, you know, approach as well. So

what is the approach in those standards -- how much of an understanding do we have there to get the full balance, and understanding then what additional value we could have. So I would expect that probably that, through CEN, that those standards might be proposed into an ISO or IEC standard, as appropriate, as a, you know, already published European standard. But if there was an appropriate -- if all the other stakeholders of ISO didn't have an opportunity to help develop that content, I'm kind of thinking of that slide that I had earlier. You're stepping in at a much later stage, so the ability to modify that content to ensure the standard has what is absolutely necessary to address the concerns that I think have been raised here, even just in the short period today, might get missed in a lot of areas.

DR. PATWARDHAN: Just add to the existing published draft PAS that we have from BSI. And the learning from the consultation, if I can say like that, is that of the few hundred responses, many are asking for -- to be less demanding. And then there are, of course, those from the pharmaceutical background companies and, of course, regulators saying, hang on, can you actually sort of crank it up a bit. So the challenge there is to -- maybe that's the question

that's being asked. There are some very important ones to address straight away. And I mentioned batteries earlier. And that's a very clear one where compliance is absolutely important to not only assure consumer safety, but also take care of some of the news, the media, sort of, that goes around it. Another one is just contaminants, and that can be easily addressed, I believe, not at a significant cost either in terms of the quality of the basic ingredients you use in the product.

And we heard about this yesterday in the entirety as well, a few times, that in nicotine, the propylene glycol, the glycerol have to be sourced and to be either European or U.S. pharma grade. So these are easy wins. And I keep on using the phrase, but the real part is easy wins for not only the industries, at significantly lower cost than anything else that would be demanded from regulation, but also from a public health point of view. So that's this opportunity to have the right balance struck there, I think.

MR. SKODACEK: Yeah, one of the things that we found when we were talking about standards for battery-powered medical devices in engaging a lot of outside stakeholders both during the workshop and afterwards is that they wanted to make sure

that we didn't put all of the devices sort of into one category and to allow flexibility for the types of devices out there, which is tremendously important given the risk levels and how these devices are used. And there is a lot of interest in having a lot of flexibility, not only thinking about what's available on the market today but about the products that are currently in the pipeline and what's in the future, because I think it's important when you might recognize a standard that it doesn't limit or basically take out a technology that might be safer or more appropriate in the future with what we know today about the products.

DR. DRESLER: Okay. Is the FDA Modernization Act, can it accommodate e-cigarettes? The FDA Modernization Act, can it accommodate e-cigarettes?

MR. COLBURN: You know, I actually probably couldn't answer that. I'd have to look to my colleagues from Center of Tobacco to -- I think there's a lot of discussion going on about how current regulations and acts can apply as appropriate. I don't think anyone is interested in trying to reinvent the wheel over. If we're referring to the part of the act that discusses the center's ability to recognize a standard for -- to satisfy any part of the act that associates

itself to medical devices, I think that's -- you know, those are tools that the Agency is aware of and familiar with. And I think, you know, it really kind of depends on what's the construct of the regulatory structure into which the Center for Tobacco is going to be addressing these products. So, yeah, I probably -- I'm not the qualified person obviously to answer that question, but I think -- my understanding of working with Center for Tobacco is that they're -- it's information-gathering, and they're trying to do what they feel is best to appropriately regulate the product to meet the needs of what the public concerns are and the safety factors.

DR. DRESLER: Okay. So saying that, this next one, this one is for you, Scott. When recognizing a standard, how do you ensure that you don't create a situation where the fox is guarding the henhouse?

MR. COLBURN: Fox is guarding the henhouse? So we have a process internally in our center that we set up groups that govern the different areas of science that we fall into, so whether it's a vertical area like orthopedic products, cardiovascular are very process-oriented, or a horizontal scientific area like biocompatibility or materials and nanotechnology, we have an internal group of experts that

represent what I consider the total product life cycle of a product, so something from the premarket to postmarket, the enforcement. Our biosurveillance, our laboratories sit and represent their office's point of views on a particular subject.

So when a standard is proposed or, you know, from the public or comes online from a new publication, we look at that. We look to see if we were involved, and if we were, who was the expert, could they come in and have a dialogue with us about how the standard was developed, were there some agendas on the table during that standards development process that we should be aware of, how does that standard satisfy the need. And so there's an entire process that it goes through real similar to how a standard is developed to ensure there's balance, that we have a process in order for to hear people's comments and concerns. And then if we feel that it is appropriate, we will recognize that standard as appropriate. And so the three standards I can identify in the battery area, that's exactly what we did, is we had that dialogue internally, and we felt that those standards would be the best -- for us.

DR. DRESLER: Okay.

MR. COLBURN: It's that kind of --

DR. DRESLER: Okay. Dr. Patwardhan, can one particular brand of e-cig be both Article 20, TPD, Article 20 -- do you know what Article 20 is? Okay. And medically regulated? Can they both be marketed with the same name? So let's start out with the first part of the question, because I think those are kind of different. Can one particular brand of e-cigarette be both Article 20 and medically regulated?

DR. PATWARDHAN: That's a trick question, for sure. I have to say that I can't answer it. I don't know the legal aspects of how it would sort of play out in the marketplace, to be honest. It seems unlikely you can do both; that's for sure. But this is, again, how it's been sort of the law has been made now. The way it's going to be interpreted is over the next 2 years, it's going to be transpositioned, and that's where it would be wherever and how it can be used and not used. So I don't know the answer to that, is a frank one. Sorry.

DR. DRESLER: All right. Anyone else want to try that one?

MR. SKODACEK: Well, I know with respect to medical devices, there are sometimes devices that are regulated as

medical products by FDA and also regulated by other agencies, such as the Consumer Product Safety Commission. Take something as simple as a helmet. If a helmet is used in a patient with epilepsy as a way to prevent them from injuring themselves when they fall, then it's regulated by FDA, but that same helmet when used in high school sports in a nonprofessional way is regulated by Consumer Product Safety Commission. And that exact same helmet is regulated by OSHA when used in the NFL, which is a business and a professional organization. So it's the exact same product. Things like wheelchairs, powered wheelchairs, these scooters that you see, whether they're from home use or from other uses -- I remember seeing a wheelchair that was intended to be used for going out on a beach, you know, going out into the water. It just seems like a crazy idea if you can't walk to go into deep water, but these different types of products are regulated depending on how they're used and the individual patients and what their needs are.

DR. DRESLER: Okay. This question is for you, because then I'm thinking maybe Dr. Lauterbach, you might want to -- in your opinion, do you feel the threshold of 20 mg/mL is too low? And is there a risk here of e-cig users reverting back

to smoking?

DR. PATWARDHAN: A lot of concerns have been raised about that ceiling that was introduced in the TPD, with claims that it is quite arbitrary without any scientific evidence base. Now, if you ask me my view as a company, I would say, listen, this is what the law is, and we have to abide by that. We believe that we can get products which would be meeting that requirement and still be consumer-acceptable going forward, but that means that innovation really has to be cranked up. And hopefully we can get the right parts. But there's a clear risk there, for sure.

DR. DRESLER: Dr. Lauterbach, did you want to go there?

DR. LAUTERBACH: Well, I think basically here we need to know more about the use. I know when I personally -- my own use, I use more than the 2%. I mean, I go higher than that, and I think this is a good reason for it just in terms of satisfaction. That's just my personal opinion on it.

DR. DRESLER: Okay. Well, it did say for your, you know, opinion, so okay.

Dr. Patwardhan, you showed a childproof cap, and I'm going to change that to child-resistant cap since from yesterday we learned there's no childproof, so we'll say a child-resistant

cap drawing. Is there a standard for 2015 or a suggestive cap as a standard? I'm not remembering, but I may have missed that slide. So you showed a child-resistant cap drawing? Is that standard for 2015? Okay. So let's just go in the European Tobacco Product Directive, was there a standard for child-resistant packaging; what does it look like?

DR. PATWARDHAN: No. There's expectation that it'll be childproof, but the real -- the right phrase is child-resistant for sure, yeah --

DR. DRESLER: I saw that on your slide, too, and I wondered -- so they're going for childproof?

DR. PATWARDHAN: Yeah, but that's again, practically, that expectation should not -- it has to be child-resistant, because in the past, when we propose product standards in the absence of the TPD, the idea was to have child-resistant. Proofing doesn't -- just practically would not work really. So it has to be child-resistant for sure.

DR. DRESLER: Okay. All right.

DR. PATWARDHAN: Yeah.

DR. DRESLER: Let's see. Go ahead. Okay. So if two million people who smoke switch completely or partially to e-cigarettes, what is the proportion of complete switchers

versus partial switchers, known as dual users? So, again, Sud, I think this was in your presentation, that two million people who smoke in the U.K. -- in the EU, switched completely or partially to e-cigarettes. So did they switch completely or did they become also dual users?

DR. PATWARDHAN: I need to look at the exact data, to be honest, so I can't just rattle off exact percentages, but it's a fairly large number of people who have actually completely switched out of smoking using electronic -- I believe it's about nearly 30% of the two million we're talking about.

DR. DRESLER: Okay.

DR. PATWARDHAN: Yeah.

DR. DRESLER: All right. Okay. Here is a series of alphabet soup is what you had called it. Beyond UL, ETL, CE, FCC, and CSA battery and testing, device testing and their standards, what else do e-vapor products need? So batteries, so maybe battery person -- yeah --

MR. SKODACEK: So a bunch of acronyms, and then what's the question?

DR. DRESLER: So and their standards, besides all of those standards, so there's one, two, three, four, five battery and device testing and their standards, what else do e-vapor

products need? And I'm thinking that if you don't know what those initials or if those aren't familiar with all of you that -- but maybe the question is do you need more than five standards?

MR. SKODACEK: Well, I do know, I mean, in terms of what FDA does, there are standards, and there are also guidance documents that outline FDA's current thinking on certain things that aren't always necessarily binding but they do provide some insights into FDA's expectations and the regulation of products, and I think setting those guidelines out help people understand what to do and how to make better products and how to test them in all kinds of different ways.

DR. DRESLER: Okay.

DR. LAUTERBACH: Often you'll see some liquid or e-cigarette packages with all this alphabet soup of initials, but there's been no certification there about the quality of the ingredients used and whether they're stable or not.

DR. DRESLER: Okay.

DR. LAUTERBACH: So the RoHS and these other things generally applies to the electronic side, and nothing is said about the e-liquid side or materials in contact with the e-liquid.

DR. DRESLER: Good point.

MR. COLBURN: So I'm going to add on to the alphabet soup. And what I heard from -- you know, we heard UL, and you know, you could consider UL a standard-developing organization or a conformity assessment certifier for -- if you look on the back end of some of these products, you see CE on there. On the back of that television, I guarantee you'll see both CE, UL, ULC and a number of other alphabet soups. And those are conformity assessment, third-party conformity assessment practices that are done to satisfy, in many cases, some sort of regulatory compliance need, law, a European need to get onto the market, you go through this -- to get a CE mark in Europe. And so a lot of time laboratories such as UL or TUV and such are accredited through the laboratory accreditation procedures to take on standards that would satisfy a requirement in order to make through -- and it's -- to get to the market.

So there's different types of conformance. There's a basic level of conformance through assigned declaration for -- towards a standard. That's something that our center does in Center for Devices. You can have more of a conformity assessment mark. That's something that OSHA does through its

NRTL program. So someone who needs to have a certification for workers' safety such as the NFL's helmets, I'm assuming, would have to go through, because they are workers and they are protected under OSHA's laws, has to have some sort of certification.

Our own products sometimes -- if you talk about -- you know, we hear of standards wars. Well, there's regulatory overlap and regulatory wars, too, you could consider, where you come to the FDA and get your clearance for, say, an infusion pump, but you need to get cleared also for workers' safety if that's going to be plugged into a hospital, because the worker needs to be protected from electrical safety. Thankfully, we're working together as a department as much as we can with the different departments to ensure we're using the same standards and to help that out. So it's kind of the favorite answer of it depends. But it really goes into the different levels.

So, here, I think they were kind of asking about conformity assessment practices that can be employed from known standards or future standards that we develop to see is that a tool that would help assess, you know, regulatory compliance or else --

DR. DRESLER: Okay. Or it depends. Okay. For a novel product like electronic cigarettes, what is a realistic timeline for developing new standards? Anyone go for that one?

MR. COLBURN: So standard development organizations have timelines that they try to abide by. ISO recently updated its directives, ISO and IEC updated its directives, part 2 or part 1, I forget, that allows standards to come in and follow even a quicker pathway. So you could go in the ISO world in as little as 2 years from new work item proposal to publication.

It really depends on -- I hate using the word, but it depends on what's the stage of the standard when it's introduced. If you're starting off with just a scope and an idea and you have to fill it all in, you have a lot more work ahead of you. But if you come in based upon a lot of sound research, or let's say BSI submits its standard forwarded to ISO, you have a construct to work from, and so you might be able to move that along quicker as well. Each organization even in the U.S. -- ASTM has a different balloting process than AAMI, than IEEE. So it kind of -- it really falls into what's the most appropriate standard organization to do the

types of things you're trying to do. Are you developing a test method for a particular test versus a product standard, which is much more encompassing and would probably be volumes thicker than maybe just a specific test method for a toxicological method, you know, to assess something specific to e-cigarettes, so --

DR. DRESLER: Before -- let me -- because you may want to address this, too. So we heard yesterday and this morning in the public comment session that these products are changing so incredibly rapidly that, you know, what we heard about yesterday is 8 years old or, you know, it's old, right? So what the consumers are using today is different, you know, and it's different broadly across a rapidly changing product. So in that instance, does that impact what you're making the standards for if the product is evolving that quickly?

MR. COLBURN: I can try to hit that. So a couple decades ago, it was very common to see very specific quantitative standards with endpoints, and even more so, you would find design standards, which is not the case today. Today you see standards that are a little bit more process-driven. Take processes and allowances for such things as design, you know, criteria risk management processes, evaluation for human

factors and other testing principles to create that standard, which allows to establish the framework for the safety issues that we know aren't new. Those are the same issues that were there 8 years ago as they are today. And it allows people to, through other methods, describe how they're still meeting those basic safety criteria and justifying those endpoints that aren't necessarily in the standard, but has the framework of what you need to do to get there and have the -- I don't know if this is even a word -- the quantification of your results to be understood and why now you still aren't meeting that -- what is today's level of knowledge from the technological advancements, the understanding of maybe new safety issues. So the standards can be developed in such a way, and they have evolved over the last few decades to try to meet that need.

DR. DRESLER: Okay. Dr. Lauterbach?

DR. LAUTERBACH: One of the issues on test method development is, number one, once you decide you're going to do the test method and have some, you know, example, the methods you might want to evaluate is the time getting out a set of test materials out to the participating laboratories, allowing them time to run these, and then getting the results back and

having evaluation of the results. And oftentimes, the time that people would need to volunteer, the laboratories need to volunteer to get this testing done can be considerable and can be considerable overhead for their operations, particularly for the private laboratories, as opposed to laboratories in a large company. So that could be a considerable time delay even when you're trying to get out a standard as rapidly as possible.

DR. DRESLER: Okay. Any other --

MR. SKODACEK: And one of the things to consider, too, is recognizing existing standards or parts of standards which can be much quicker. Certainly, there are a lot of standards for communication between electronic devices that might apply to a smartphone but also could apply to a e-cigarette or for a battery. There's lots of missing pieces in consumer products, and there are already standards there that can be recognized to get us a head start.

DR. DRESLER: Okay. Dr. Lauterbach, you mentioned that there is ample data on ventilation toxicology of flavoring ingredients. I have seen data that 27 food ingredient flavors need further testing for ventilation. Can you expand on what data is available and whether or not the combination of

flavorings under heat are likely to cause new harm risks that are not already comprehended in the data available?

DR. LAUTERBACH: Well, first, I think we're talking about inhalation toxicology, okay? And I mean, one of the things we need to look at here is the work that's been done in conjunction with the development of cigarette flavorings versus those that may be satisfactory for e-cigarettes, and there are things that I would allow as a regulator or as a company toxicologist, I would allow in a cigarette flavor that I would not want in an e-cigarette flavor. For example, reaction products, I wouldn't want anything in an e-cigarette flavor that would essentially be nonvolatile or give me undefined pyrolysis products. So I think that needs further clarification about what particular concerns they're asking.

DR. DRESLER: Okay. All right. Handwriting.

(Laughter.)

DR. DRESLER: Could -- I was thinking it was gold standard, but it's could standardization alleviate the need to make extensive data submissions within product approval applications, and what are the limitations? So could standardizations alleviate the need to make extensive data submissions within product approval applications, and what are

those limits?

MR. COLBURN: So I'll speak to it now as it relates to our processes in Center for Devices, where we have, you know, the most common product that we see, submission that we see is a 510(k) for your typical Class II, you know, devices, which is lower than the Class III, where you would submit a premarket application. But through that, the process that our recognition of a standard does is to help, you know, and it's actually written into the law, is that in lieu of providing all the background data, if we recognize a standard, what we're communicating is we understand that test method, we understand the process, we may -- and if it's a full standard, a complete standard, we even agree to the endpoints that that standard has built into it.

And so depending upon the type of standard that it is -- if it is a full -- like, say it's a test method with endpoints, a declaration of conformity may satisfy that part of the regulatory question that we would ask versus having to see the full test report. If it's a standard on risk management, you know, ISO 14971, if you said I declare a conformance to that, we would say, okay, let's see your risk assessment and what did you use, an FMEA, another model, but

it doesn't stop there.

And I think the same thing goes for electrical safety. You don't declare a conformance to electrical safety in the current edition, because the current edition employs a risk management process into it, where the industry navigates how they chose which parts of that massive 343-page standard applies to their specific product. But that dialogue doesn't stop with just saying we comply. But it really does shrink down that, you know, what could be volumes of information down into a summary test report possibly, or a summary test report with maybe some additional annexes to describe maybe a deviation they had to employ into the standard because of new technology that was employed into their device.

And so that's the flexibility that the Center for Devices has, is that you can use this standard, you can declare -- you can use the standard as published. You can even have the communication with us on if you had to deviate from that standard because of new technological advancements but that standard still applies best to your product. But we need to have that justification discussion on how we amended that -- or altered that standard. So it still works as a great tool to shorten all the back and forth that goes across if you

didn't have that resource.

DR. DRESLER: That makes sense. Thank you.

MR. SKODACEK: And I think I can give one example for battery-powered devices. And there's a requirement for the temperature not to exceed 41 degrees for an implantable device. And that's in the standard, and it's the one I actually -- I showed on the screen. But, in fact, the testing methods to do that are not described in the standard with sufficient detail to know whether or not the manufacturer is going to get the result that you expect. They could have put the pulse trainer in a different medium where the conductivity is different. They could have shorted the battery for a short period of time. The battery could have been partially depleted. There's all kinds of things that while intention can go wrong in your testing such that you think you're fulfilling the requirements of the standard, but in fact, in other worst cases, you would not.

DR. DRESLER: Okay. Do we have any other questions? That's it for the questions coming through?

(No response.)

DR. DRESLER: All right. And I have a yellow light, meaning that we're kind of near the end. So thank you very

much for the speakers and panelists. Thank you very much.

(Applause.)

(Whereupon, at 11:22 a.m., a luncheon recess was taken.)

A F T E R N O O N S E S S I O N

(12:33 p.m.)

DR. DRESLER: Okay. Let's get started on the afternoon session. In the afternoon session, we'll start off with Protective Packaging, and our first presenter will be Dr. Joseph Hotchkiss from Michigan State University, and he will be addressing General Packaging Considerations.

Dr. Hotchkiss?

DR. DRESLER: And you probably saw I didn't -- forward and back.

DR. HOTCHKISS: Okay.

DR. DRESLER: And if you want the mouse --

DR. HOTCHKISS: Well, we'll see. Thank you very much.

First, for my disclaimer, I have no financial interests in

anything related to anything that I've heard so far, and I am, however, a former FDA employee and currently a special government employee, which if you want to know what that means, it means that you work for free.

(Laughter.)

DR. HOTCHKISS: And it also means that I have access to all your cell phone information.

(Laughter.)

DR. HOTCHKISS: That goes over in Europe like a lead balloon, I'm telling you. See what they do in Europe over that.

(Laughter.)

DR. HOTCHKISS: Packaging and e-cigarettes. I'm going to try to do a few things, and one is to generally tell you some things about packaging, and most of you are going to kind of glaze over right away, because you're going to say, hey, listen, I know that I use somewhere between 8 and 12 packages a day and throw them all away. I know about packaging. But there's a lot more to packaging, I think, at least I'm going to try to convince you, than you know. And there's a certain amount that applies to this category of product.

So I'm going to talk about, first of all, define what is

packaging in a very quick way so you have some understanding, at least, so we agree what packaging is. What's generally required of packaging of consumer goods, and particularly going to then focus that on e-cigarettes and products, and then further focus that on things like safety marketing, informing, and so forth that I think has some applicability to this particular product category.

I'm going to talk a little bit about how companies, including e-cigarette companies, develop packaging because I want you to understand the sophistication of the marketing aspects of packaging and the development and how it works. What's the role of packaging in marketing and use in cigarettes?

Packaging, as I defined it, is a technical system. The first thing to know about it, it is technical. It's a technical way to distribute, market, and deliver products. It's certainly, when we think about packaging, or at least most of you think about packaging, you think about the thing that contacts or holds the product. There are a lot of other packaging, some of which you hardly ever see, but the packaging is a pretty complex process with a variety of objectives. I'm going to talk mostly about primary packaging,

that is, the packaging that contacts the product, the packaging that the consumer sees, because I think that is perhaps the most germane to our discussion.

In this context, if you came from Mars and looked at e-cigarettes, I think you'd say, oh, yeah, that's a package. If we were talking about a pharmaceutical packaging, that is, something that delivers a pharmaceutical, we would clearly call that a package, kind of thing. And after all, that's what an e-cigarette is doing, is delivering something to be consumed by human beings.

We have a number of demands of packaging, and I like -- well, I like this list for a couple of reasons. One, I like it because I made it up, but beyond that, it describes what we expect out of packaging. We have a whole bunch of things we expect out of packaging, and as product manufacturers, these are very carefully considered. You got to contain the product, protect it, safety, facilitate product use, certainly market it, persuade and educate people to buy it, identify, production efficiency is a very important product, environmental impact is important these days, and economic costs. I'm going to ignore some of those, and some of the ones that I have an asterisk on I'm going to talk about a

little bit more, and then a couple of them in more detail. But it's important to understand that with all of these kind of competing requirements for packaging a product, including things like e-cigarettes and the e-juice -- I like that name, e-juice -- packaging those, we really do have a optimization process. We cannot do everything perfectly in this realm. So we end up making some choices that are really optimizations.

Protect the product. Obviously, damage during distribution, protect the product from environmental contaminations, things like microorganisms, other chemicals and those kinds of things, kind of the square one in packaging. And how does this apply to the e-cigarette business? The e-cigarette business is a pretty complex product. You can find, I think, much of the packaging, at least for these kinds of products, is more akin to the electronics industry than it is to other kind of consumable products in this thing. It's quite complicated -- let me go backwards -- quite complicated packaging that does a whole variety of things. Hence, the design and the effort. And if you don't know, packaging is really very expensive material. Typically not for electronics, but for other consumer products, the packaging usually costs more than the

ingredients to make that product.

Some safety-related issues, and particularly, those that I think revolve around or impact some of the discussion about -- that's been going on today and yesterday around e-cigarettes and products. Top of my list would be child and tamper resistance. I'm going to say a few things more about that in a minute, and you'll hear -- after me, you'll hear some even more information on this particular topic.

Potential for biological contamination, very interesting. I haven't heard much about it from anybody, but it seems to me there is a potential for biological contamination, and certainly, you wouldn't want to breathe in certain kinds of biological contaminants that might be viruses or other kinds of things, and I haven't seen -- I tried to find some research on this, find nothing, except that I know that glycerol kinds of compounds are typically what we use in microbiology to preserve microorganisms for long-term storage, and so forth, and so I kind of wonder about what the biological consequences, if any, are.

Harmful misuse of the product. Usually in the world of packaging, we take this into consideration that not all people read the label, not all people buy the product for its

intended use, that a number of people buy the product for other kinds of uses that might be harmful. And typically through packaging, we might try to reduce those harmful uses of the product. I think this is important for the industry to think about as well.

Composition of consumables. There's been a lot of discussion about this and a lot about inhalation, and I'll say something more about that in a moment. Much of the discussion has been around certainly nicotine and some of the contaminants in nicotine, but also a lot of the discussion around the flavorings. And I've heard some interesting -- I'm going to give you some numbers on flavorings. Flavorings are much, much more complicated than I think most of you understand.

Also, migration of packaging and device components to the consumable product. We've heard a little bit about this, but for virtually all consumable products and particularly those regulated by the Food and Drug Administration, that is, foods -- actually, it's very interesting around foods because the Food and Drug Administration receives more petitions or more information around the transfer migrants than they do the additives that are put into food. I think in the last

5 years, there have been two food additive petitions put before FDA and several hundred indirect additive kinds of things, things that potentially migrate to foods. I'll tell you what the list of those things is in a moment, and you'll see that they are considerable.

Some numbers on what is -- I hear the word approved food additives. FDA actually approves very few food additives. They issue things like letters of no objection and no response and those kinds of things. There is a very special category of things called approved food additives, but it is very limited. As I say, in the last 4 or 5 years, I think there have only been two petitions for food additives.

The numbers. FEMA, which is not the emergency response people, but they may think so -- it's the Flavor Extract Manufacturers Association -- looks at flavors and basically GRAS -- self-affirms them as GRAS through a committee. They've done this since 1961. I've worked with this group. I've worked with JECFA on this. There are about 2,800 approved food flavoring ingredients. Most of those are used in combination. So if you're flavoring some of the products that we're going to look at, you're going to use several of those compounds in there.

I heard that here is some toxicology done on these, some inhalation toxicology. And as I dig around and look for the inhalation toxicology, it mostly is to add the flavoring to a tobacco product and then evaluate that tobacco product most often in an in vitro system, but at times in an in vivo system. I found one list that listed 170 such flavorings evaluated, 170 out of a potential -- if you're only using FDA-approved or FDA-regulated or FDA-knowledgeable additives, GRAS substances, you have 2,800, and 170 have been tested. Very interestingly, in the testing process is typically to add them to tobacco and then test the -- smoke the tobacco and then test the condensate from that, or something, which seems very strange to me. From the food side, that's like putting a flavor in a beverage, feeding it to rats, and say, you know what, the flavoring must be safe or the coloring or the preservative or whatever because the rats did just fine drinking the beverage. That's not the way it's done. Normally, you would test the material by itself.

Indirect additives. Those are things that get into food or can get into food from contact surfaces, from manufacturing processes. There are about 3,230 some of those chemicals known. Food contact notification additives. That means that

if you are making a container in which you are going to put a food contact product or, by extension, drugs in, then you -- and it is not on the list, then you must notify FDA that you have a new food contact material, and they will make an evaluation of that. There are 646. So if you are using a food quality container for an e-juice, for example, the potential is for some 646 components to leach to that material.

Non-approved food contact materials. Boy, the number is hard to say, and it's almost infinite. And you have to understand, particularly in the world of plastics, but not just plastics, other materials as well, you can roughly divide them into two categories, those that are formulated and intended for food contact or consumable contact and those that are not. And those that are not are made with different kinds of materials because they're cheaper than those that are. So I think the issue of migration is one that bears some thought.

Child-resistant packaging. I said I'd mention this, and I kind of looked around. I see, if you look in the upper left-hand corner, that one does have a warning label on it. There are child-resistant containers available. I don't know the extent to which they're used. I don't know if they actually

meet the Consumer Product Safety Commission requirements. They make no real case for that. There are ones that apparently are not. And this seems to be a rather important issue for me particularly for these products. If you look in the lower right hand, I really like this product because this is some kind of bomb vapor. It's a cinnamon flavor. And this took me back to my childhood when we used to go to the drugstore and buy cinnamon oil and consume cinnamon oil just to see how brave we could do that. It seems to me that that is a very child-friendly kind of thing. As a matter of fact, if you look at what they say about this, it says, "Radiate your taste buds with our Blast Radius (hot cinnamon) E-Liquid. Blast Radius is similar to Big Red gum and Red Hots" -- so the comparison is made to common candies consumed by children -- "but simply better. Your tongue will be left with" -- well, you can read the rest of it, and you can go to that -- and if you want to see it down there.

I got kind of interested. This stuff is apparently formulated in different levels of nicotine up to 24 mg/mL strength. I found a nicotine toxicology site that said that LD50 in humans is some -- a 50 to 60 kg human is something like around a mg/kg. That may be a little low, but if you

kind of do the math, if you weigh 10 kg, for example, or 20 kg, you're pretty close to the LD50. If you don't know what LD50 is, that means the dose that's going to kill 50% of the people that are -- or the animals or whatever you give it to. So that's a pretty blunt stick to look at.

Some companies apparently see it. This is something called liquid -- Italian flavored. I never really understood. I was trying to understand exactly what Italian flavored means. I don't know if that means you taste like an Italian, or I'm not sure what that means, so it's a little strange. But they did understand the role of packaging. You'll see it says there in the right packaging, "This bottle is made of high-strength food grade material that will not break or leak." They say it's food grade. They also use it to -- I said one of the requirements of packaging that you really want to do is product use. And they show that they have a way to use this that really works well in filling your little device.

Packaging claims. All kinds of interesting claims that you see floating out around there. This is how -- E, I don't know what this is. But it says it "uses a premium FDA-approved natural and artificial flavorings to offer rich taste." I'm not so sure that FDA would really agree that they

approve flavorings. Most flavorings in foods are GRAS, which means FDA basically looks at it and issues a no objection kind of letter. They don't actually approve those.

I also found one -- I'm going to ask at the end of this meeting for my FDA seal, because I understand FDA is now putting out seals that say you can get a seal on these e-juices that says FDA says they're okay. I don't think I'll get that seal, will I? I've never heard of that.

This is an interesting example of what I said about using packaging for the product. It says, "This Freedom Pack gives the user a top-notch experience and allows them to make an easier transition to e-cigarettes."

And, of course, packaging is used to persuade and educate and market. Actually, I put this in here because if you can't remember anything else about the guy that came and talked about packaging, try to remember this. Nothing in consumer packaging happens by chance. Every little corner, every little speck of ink, everything on that container is well thought through, and I'm going to show you in a second how well. The goal is to connect you to a product.

How many of you own an Apple product? I have one on. How many of you have an Apple product package in your closets or

someplace? You're so connect -- why? Because you're so connected to Apple. Apple is very famous for connecting people. On the other hand, if you buy a Microsoft product, you are not going to put this clamshell in your -- you're going to scream at them and holler at them.

(Laughter.)

DR. HOTCHKISS: Packaging connects us very much -- oh, I wanted to see if I can show -- oh, here we go, if I can -- there we go, if I can find it on here. Oh, it may not -- there's a -- I don't know -- there is -- I wanted to show you there is a very sophisticated set of tools that design packaging in a virtual sense but put it on a real store shelf. So designing these things to emotionally connect you with is a very sophisticated business these days, and virtually everybody of any size in the consumer products industry is using these tools.

They use colors. What colors say exotic and expensive? Obviously, these. Black is a favorite. Gold is a favorite. Anything metallic. I noticed the animal skin on the left is used as well.

So there are a lot of things that are used to market products. Of course, if you want to think -- for some reason,

if you want to think vaporing is an environmentally friendly thing, you can buy -- or you want to be environmentally friendly, you can buy Green Smoke with liquids that are "exceptionally robust and accurate." I don't know what an accurate -- I guess they mean they taste like what they say they're going to be like.

Your target packaging. I particularly like this one. If you're like I do, make your living hanging around with 18-year-olds, you know that Red Bull is consumed in huge quantities by college students, unbelievable quantities. And, of course, somebody in this business has determined that that's a good thing, and now they apparently have a Red Bull flavor. One of my favorite ones is vanilla cupcake. Lots of fruit ones. I like the fruit ones, but vanilla cupcake, I can't imagine wanting to taste something -- by the way, if you don't know, you can't taste anywhere in your mouth or your lungs any of these things. All of your taste occurs right here in your forehead kind of thing. That's the only place you can taste. You have receptors there.

Imitation? Certainly. Packaging has imitated other kinds of things. You got to stare at that a little bit, the one on the left a little bit, to see the juxtaposition of those

products.

Accurately communicate. And I think this is an important area for FDA to think about. Authenticate. It was mentioned a little bit. These products will be knocked off. They're probably already being knocked off. The faults or counterfeit products are wide across the product categories. And particularly, and it's kind of funny, because as I understand it most of these are made in China anyway, and that's where most knockoff products come from is China. And there will be cheaper quality products with different kinds of names.

Quantity of contents, how much is in there; the use; the risks associated with it; warning and limitations. You saw a couple examples where people do things on that. Who the manufacturer or distributor is; and importantly, recall codes. If you're selling a consumable, you got to have a recall code on it in case something goes wrong with that. And you saw that nicotine levels can be all over. So if you have a product that's two or three times the nicotine level, you want to probably get that product back.

The last one, and I just quickly mentioned it because it gives you an indication of how -- the size of this industry. And this is a machine. If you wanted to go out and buy this

-- I said one of the requirements of packaging is it has to be done efficiently. This is probably a quarter of a million dollar machine built specifically just to package e-cigarettes. So there is an investment in the process of making those. It's a Chinese company.

So some conclusions. There certainly are health and safety implications of packaging for e-cigarettes and associated products, clearly things like migration, child resistance, especially of these flavored juices that strike me as simply targeted towards young people. Labeling, that's an important issue. Packaging is a key factor in the marketing of cigarettes, and certainly -- or of e-cigarettes, and certainly, that's important to think about. Generic packaging would certainly reduce appeal. We want to grow markets, broaden appeal. E-cigarettes use packaging very similar to other products, and I think you can learn from those other products.

Thank you.

(Applause.)

DR. DRESLER: Okay. Good. Our next speaker is Dr. Quinlan from the American Academy of Pediatrics, speaking on Liquid Nicotine Poisoning: An Emerging Threat to Children.

DR. QUINLAN: Okay. Thank you. Good afternoon. My name is Kyran Quinlan. I'm an academic, practicing pediatrician in Chicago at the Rush University Medical Center. And, first, I want to thank you very much to the FDA, Dr. Dresler, Dr. Durmowicz, also Karen, for organizing this and giving us time.

I represent the American Academy of Pediatrics here today. And I'm going to be talking about some recent data regarding child poisonings. We're going to go over child development and the risk of poisonings, the history of protecting children from poisonings and in particular this issue, liquid nicotine, and the current challenge. I have no pertinent financial relationships to disclose.

Just so you know, the American Academy of Pediatrics is a professional organization of 62,000 pediatricians across the country. We're all dedicated to the health and safety and well-being of infants, children, adolescents, and young adults. Our organizational structure includes committees, sections, councils, and I chair the Council on Injury, Violence, and Poison Prevention for the American Academy of Pediatrics.

So I'm here today to address an important emerging issue,

an urgent concern that we have regarding child poisonings related to the concentrated liquid nicotine that's used in e-cigarettes. It's a significant concern, and I want to make sure you understand that currently U.S. children are at the lowest historic levels of child poisoning. We came from about four or five hundred kids a year dying of poisoning ingestions. We are now on the order of about 36 child deaths a year that happen from poisonings. And this did not just happen by chance. But things have changed, and we have a new poisoning risk. And that's what I'm here to talk with you about today.

Beginning in late 2010, we started to see poisonings related to this product, the liquid nicotine in particular. And these poisonings are increasing rapidly. Many of you, I'm sure, have seen this. This was published in the *Morbidity and Mortality Weekly Report*, which is a weekly thing put out by the Centers for Disease Control and Prevention. And these are calls to poison centers for cigarette or e-cigarette exposures by month. And it began in late 2010. That's when a code was finally introduced so that poison control centers could report on this. So we started to see some numbers just beginning in the end of 2010. Those numbers continued and just began to

trickle up in 2011. In 2012 they increased some. In 2013 they increased much more significantly. This goes up just to February of 2014, but the numbers are starting to increase in a much more accelerated fashion.

I should mention that the lower line that is the solid line, that is the number for exposure calls to poison control centers in the country for exposures to e-cigarette and the nicotine products. The top hash line is just a comparison group. That's the calls to poison control centers for exposures of kids to regular tobacco-burning cigarettes. So a kid eats a cigarette, and there's a call to the poison control center. Those numbers have basically floated around, around the same number, haven't really changed much. But what we are seeing a change in is the exposure calls related to this product.

This is a little more detail and a little more updated of the same data. So, basically, in 2011 we had about 270 calls. In 2012 there were nearly 500 calls. In 2013 there were 1,500 or so calls. And then in 2014, up till Halloween, just until the end of October, we had a total of over 3,300 calls. That does not include the last couple months of this year obviously.

So we know from history that young children have always been at the highest risk for ingestions and poisoning. And we know, too, that kids under the age of 5 are typical victims of poisoning. Ages 1 to 2 are the peak age risk group for virtually all ingestions. So 1 to 2 year olds. And it's aspects of their normal development that lead to this. And it's understandable. It puts them at risk. We know in this product, in particular, that bright colors, attractive packaging, some of the symbols that are used, there's a lot about this product, the liquid nicotine product, that appeals to children and naturally would appeal to a child.

You know, I want you to -- many of you probably have children or maybe you have nieces, nephews. Think about a 12-month-old child; 12-month-old kids sit at their high chair, Cheerios, they pick up things, they use their hands to feed themselves. That's a 12-month-old child. A 15- to 18-month-old child is able to start using a spoon. Their fine motor skills are excellent already at this age. At 2, they're very good at manipulating things with their hands. When you think about a 9 to 12-month-old child is starting to pull to stand, may begin to take a step. They very soon take their own steps and are walking and very rapidly begin to climb and are able

to climb. Their fine motor and gross motor skills put them at tremendous risk for access to unsafe and hazardous products in their environment.

The one thing that's missing is their understanding. Their cognitive development does not allow for them to understand the serious and perhaps lifelong or even fatal consequences of their actions. These are children that would walk directly into traffic if they were allowed to. This is normal. These are normal, healthy kids, and that should be allowed in their environment to live that way. They learn by play, and they experience the world and explore. And that's part of being a 1- and 2-year-old child. You know, this is the age when parents in my practice are the tiredest sometimes because they are chasing those children around all day trying to keep them from killing themselves. That's normal.

So because of their development, young children are at a high risk of exposing -- so there's a lot of hand-to-mouth behaviors I meant to mention, too. So they're very likely to get things in their mouth. They can do it. They're at high risk for the oral and mucosal exposure that you guys have heard about. They definitely are also at a high risk for dermal exposure of this product. Kids this age use sippy

cups. And the reason they use sippy cups with the valve is because they spill all the time. This is normal at this age. So if a child is drinking a nicotine liquid product, they will spill it. And they'll spill it on their skin, on their face, on their arms, wherever, and wherever they spill it, it will be also absorbed, so adding to their toxicity. They are also nicotine naïve. They do not have previous exposure to nicotine. It's much easier for them to begin to achieve toxic effects of the drug.

The LD50 as you guys have just heard about, the median dose for a lethal exposure is not perfectly known. No one has done human studies to prove exactly what that is. Based on everything that we have, we know that the LD50 is very likely between 1 and 13 mg/kg of body weight. One and two-year-olds do not have much body weight. It doesn't take many milligrams per their kilogram. It ends up being a small number in terms of overall milligrams. And we'll get into that in just a second.

I think many of you are probably aware of the *New England Journal* producing or publishing this case report. It's very unusual for the premier journal in the world, medical journal in the world to do this. You know, a case series, maybe;

studies, of course; but a case report that involved one case. I think it's a testament to the concern that the medical community has about this issue. So this was a 10-month-old baby, child that was brought into the emergency department for -- after having swallowed what was thought to be "a small amount" of the liquid nicotine product. But you see this picture is actually from the *New England Journal*. On the right is the product that the child drank from. And you can see it's hand-labeled. It says 18 mg, and we presume that that's 18 mg/mL. The child came vomiting, was tachycardic, meaning the heart was racing. The child was in respiratory distress and also had truncal ataxia, just means that the child was unsteady, was neurologically affected by this. This child in 6 hours was back to normal, got to go home, had supportive treatment at the hospital and did well, and was very fortunate.

But let's look about what does it take to kill a young child? How much nicotine would it take to have that previous report not be so fortunate? This table shows in the first column on the left a concentration of usual products, 18 mg, 24 mg, or 36 mg/mL. In the middle column is translating that for a 10 kg 1-year-old, the usual weight, about the 50th

percentile for a 1-year-old is about 10 kg, or 22 pounds.

So let's translate how much of each of these concentrations gets you to the LD50. And depending on the range of the 1 to 13 mg/kg, say, for the 18 mg concentration, so we're in the top middle now, top middle column, that 0.6 to 7.2 mL is what would be required to get in that range in terms of volume of that product to get to the LD50 for a child that is a 1-year-old. 7.2 mL is just little under a teaspoon and a half, to put it in plain English. If it's a 24 mg/mL concentration, we're talking 0.4 to 5.4 mL. 5.4 mL, the upper limit of the LD50 is about one teaspoon. If it's 36 mg/mL, which is sold, 0.3 to 3.6 mL. That's less than one teaspoon. We're talking about a sip of these products that could kill a child.

So what do we do about this? We know that there's been successes in the past, and the way we are right now at historically low levels is, in particular, the success of the Poison Prevention Packaging Act of 1970. We know from yesterday's talk by Dr. Boja from the CPSC all about that act. We know it was passed in 1970, that it basically requires hazardous household products to be in special packaging, packaging that is both child resistant but adult friendly.

And this was driven, in part, by the number of aspirin ingestions and deaths. We knew at that time that easy access to a lethal dose and quantity of a serious product for young children and a commonly owned product was a deadly combination. And I think that that, what I just said, is unfortunately becoming more common again with this product. These are commonly owned, there is a lethality to them, and access is clear without child-resistant packaging.

So the Poison Prevention Packaging Act was a success, and there is a real need for action. The urgency on this issue cannot be overstated. There has been a death in Israel, as you all might know, probably know, back in May 2013. We know that an Israeli child became the first fatality in the world, as far as we know. We know, too, that without child-resistant packaging, the children would become exposed and will begin to clarify the danger to us. And what I'm trying to say is if we wait, you'll start to see the effects, and then we'll learn perhaps the real LD50. And this is not the right way to do it. This is backwards. This is not prevention. It's almost like how I take care of patients and they have lead poisoning. I draw their blood in clinic. I find the lead in their blood. And then we realize that their home has lead in it. It's

backwards. I've used the child as a lead detector, and that is not the way we should be working.

There is another issue that I am sure you've heard about earlier today. I know you heard about this. And that is about the death in this country. And I apologize for -- this slide is now outdated. I sent it in 5 days ago, but it appears to only be a matter of time before the U.S. child death, and in the time since I sent in these slides, it unfortunately has happened. In the Albany *Times Union* yesterday, it was reported, and I'm reading: "A 1-year-old boy died Tuesday after police said he swallowed liquid nicotine, the chemical used in electronic cigarettes. Emergency workers were called to a home on Garfield Street at 4:06 p.m. Tuesday after getting a call that a child was unresponsive. An ambulance took the boy to Little Falls Hospital, where he was pronounced dead at 5:53 p.m. Police are still investigating the death but said they believe it was an accident."

Obviously, this is so new we do not know all the details. We do not know the exact mechanism. We do not know how he accessed the fluid. We do not know whether there was child-resistant packaging, but what we do know is that this child is

dead, and I fear it may just be the beginning.

So what do we do to prevent these? What do we do to protect children? Child-resistant packaging must be required for all nicotine-containing liquids sold for e-cigarettes. Before this is regulated even, this should happen voluntarily. No retail or online source should sell this product without such protection. The amount of nicotine in any individual bottle should not be enough to kill a child. Flow restrictors. On the bottom here, there's a picture of bottles that have flow restrictors. They're just a design element in the lid, in the top of the bottle. It limits the amount of liquid that can come out at any one time. It makes it much harder for a young child to get a lot of liquid out at one time. And research by the CDC and the Georgia Poison Center has demonstrated that these flow restrictors are effective in thwarting young children from gaining rapid access to bottled liquids. Really, this limits exposure and gives parents time.

The science is very clear. The history is very clear. And, tragically, history is beginning to repeat itself. As the electronic cigarette industry rapidly expands, concentrated liquid nicotine is a new poisoning threat which has started to kill young children. Let me be very clear.

Education and supervision are not the answer. We know what works. Even before it is required by regulation, all nicotine products must be sold only in child-resistant packaging.

Thank you.

(Applause.)

DR. DRESLER: Because we are running a bit ahead today, I am -- if there's any questions for either Dr. Hotchkiss or Dr. Quinlan, if you want to pass the cards. Amy, do we have any questions? No? I'll even go out and get my microphone if there's any questions for either of those two speakers? No? We do have one? Okay. So thank you very much, both speakers for excellent presentations.

Thank you.

We'll go ahead and move forward to the next session, please. The next session is Environmental Considerations. And we'll have an Overview of NEPA, the National Environmental Policy Act, by Dr. Hoshing Chang, who's from the FDA Center for Tobacco Products.

Hoshing?

DR. CHANG: I know I have to always adjust the microphone before I stand in front of any audience. I just need a few inches taller.

Hi, good afternoon. My name is Hoshing Chang, and I am one of the scientists in Office of Science in Center for Tobacco Products. And it is my greatest pleasure that I came here to do a really mini introduction about this environmental considerations action.

Well, I thought this is a really excellent flow in terms of the topic to follow by protecting our children, then, now, as think about protect our children's children, the next generation, that is, to think about the environment.

So the title of my talk for today is Assessing Environmental Impact of Electronic Cigarettes - FDA's NEPA Responsibility.

Okay. Short disclaimer. This information and this material is not a formal dissemination of information by FDA and does not represent Agency position or policy.

My presentation outlines are twofold. Mainly, I'm going to briefly, really, really briefly talk about national environmental policy and FDA, and secondly, is potential environmental impacts of e-cigarettes associated with -- to harvesting of tobacco products, manufacturing of tobacco products, use of -- I'm sorry -- harvesting tobacco, manufacturing electronic cigarette, use of electronic

cigarettes, and disposal of electronic cigarette after use. Most of my talk is, actually, a lot of question marks.

So what is NEPA? NEPA is National Environmental Policy Act, and the definition of NEPA in -- it is a national policy which will encourage productive and enjoyable harmony between man and his environment.

So what is the purpose of NEPA? Well, NEPA is to prevent or eliminate damage to the environment and biosphere and stimulate health and welfare of man. It is also to enrich the understanding of the ecological system and natural resources important to the nation. And, thirdly, it is to establish a Council on Environmental Quality situated in White House.

Okay. So what are the FDA decisions subject to NEPA? Mainly, there are two. One is issuing regulations. So when FDA proposing a regulations, FDA -- it is FDA's responsibility to prepare a NEPA document to assess the environmental impact. And the other one is to provide permits for private actions. So when FDA is allowing or approves certain products to be on the market, FDA is required to have a environmental document to be prepared.

All right. So what are the potential environmental impacts of electronic cigarettes? So our thinking is based

Council on Environmental Quality's guidance, and also general concern of FDA-regulated product based on FDA's environmental consideration history.

So let's start with -- ask the first question. What is the source of nicotine that is incorporated in e-juice? So nicotine can be synthesized chemically and also can be extracted from tobacco products, tobacco plants. So here I provide an example about when it is extracted from tobacco products. Then we will consider what is the pollutant and what is the byproduct emitted during the process of extraction. Then we also ask the question, so will there be a cultivation of tobacco altering happens in the land use. And, of course, there are some other components are incorporated in electronic cigarette, so I just provide example of nicotine.

So when all those components are being put in together to form or to manufacture electronic cigarette, and what is the manufacturing process of an electronic cigarette. It can be manufactured in a small business setting or it can be manufactured in a mass production. So usually the environmental emission, if that is emitted from a large facility, it does qualify under the TRI, the EPA environmental emission program, and that emission can be captured under a

database established by EPA. But in some situation, if that is -- if the product is manufactured in a home setting, then we may not be able to understand the pollutant emitted during the manufacture process.

Then we also consider -- we also evaluate what will be the impact on indoor air quality. What will be the impact on nonuser, particularly, about secondhand vapor and thirdhand vapor exposure. And I believe this probably going to be touched upon in a following up workshop, so we're not going to discuss this further here.

And, finally, so how does the product will be disposed after use. In example of electronic cigarette, would a battery be recycled, and how is the cartridge to be disposed by regular users, and what would be the environmental impacts due to those behaviors.

Okay. Based on some literature review in-house, we figure that while there is actually a huge research gap in considering the environmental impacts as a result of manufacturing, harvesting of tobacco, and also use of -- and also disposal of electronic cigarette after use. There are some articles, some research published to discuss about what is impact on indoor air quality, and we think the result is

really inconclusive at this point. Of course, it's going to be discussed later on in following-up workshop.

Okay. So to conclude what my brief introduction of this environmental consideration section is, we actually have a lot more research needs to be done in this area to understand the environmental impacts due to the harvesting of tobacco product, manufacturing of the electronic cigarette, and use and disposal following use of electronic cigarettes.

And I'd like to thank you for your attention.

(Applause.)

DR. DRESLER: Okay. The next speaker is Dr. David Meyer from the Environmental Protection Agency, and he will be speaking on Understanding Environmental Impacts Using Life Cycle Assessment.

DR. MEYER: Okay. I will move the mike back up, I think.

All right. So as she said, I'm with the U.S. EPA. Hold your boos to the end. Let's see. I am here with my agency's approval, so therefore, I can't have any sort of financial or ethical conflicts of interest. And the things I say probably if you called people at the EPA, they'd just say they don't know me. So here we go.

I was actually asked today by FDA to come in and talk

because in the group I work in and our National Risk Management Research Laboratory, we look at using life cycle assessment as a way of understanding the environmental impacts of products, chemicals, processes, and that's because it's something that's becoming big with this idea of moving towards sustainable decision making. The talk today, I typically talk like 50 minutes to an hour on this subject, so you guys are getting the much-abridged version in like 20 minutes or less. We're going to fly through a little LCA 101 and then just talk about some of the specific things you should think about, the challenges if you want to look at doing life cycle assessment with the e-cigarettes.

I always throw this up when I'm talking to mixed groups, including toxicologists and risk assessors, and that's because the term life cycle has a very distinct meaning to all these different groups. When I speak, I am usually referring to a product life cycle, meaning going from taking the materials out of the ground and all the way around to the end of life and what we do with it. But I understand for certain people, you say life cycle, and this might mean a species life cycle, going from birth to death. If you talk to a risk assessor, it's actually a chemical life cycle, and they're interested in

what happens from the time that something is released until it has some sort of effect on the environment.

In general, we think about assessing the environmental impact because as a society, or multiple societies around the world, we're becoming aware that we have a pretty symbiotic, you know, relationship with the natural earth, and we need things from the earth to survive, and so we need to take care of that. Some of the questions I always throw out there that gets it beyond sort of the health discussion in general are things like do we have enough material resources to support global scale production of products? One of the big ones I would throw out there is people might remember there was the bit rare earth element scare, and probably three or four years ago, you know, everyone was panicking that China was cornering the market, they were going to cut us off, and then we wouldn't have our iPhones and our laptops, which probably would have been a big civil revolt based on how technologically obsessed we are as a society. And then other questions that people want to know is how stable are the chemicals and all these new types of materials that we're making as we go across the life cycle. The big example here is typically nanomaterials and that people want to know -- we

have all these wonderful nanotechnologies, but if they're released, the last question there, what happens, is it going to kill me?

We have multiple tools we can look at for environmental impact assessment. I could probably have slide after slide, going through them all. Probably the two most common now are risk assessment, which is sort of what's standard at the U.S. EPA, when we think about human health risk assessment and ecological risk assessment. And then there's the life cycle assessments that I work in. And it's the focus of the talk today.

For a life cycle assessment, the reason that my colleagues and I probably got into working in this area, at the heart and soul of it all, it's basically a tool that helps us identify and quantify natural resource usage and releases to the environment across the product's life cycle. And if I know about all this sort of inventory, I can easily convert those into impacts. Once I understand the impacts, I therefore have the opportunity to improve products and perhaps create more sustainable societies.

One of the beauties of life cycle assessment is it often can lead to this idea of unintended consequences. And the

example that my mentor always gave me and that I tend to give people is biofuels. And that's, you know, it was the big deal, we need to convert to biofuels. It's the green, sustainable, renewable technology. So people said, well, I guess we should prove it, and they started doing life cycle assessments, and one of the things that cropped up that no one had thought about was, you know, if we start having to grow all of these biofeed stocks, the runoff from all of the agricultural production processes is going to create this giant hypoxic zone in the Gulf of Mexico, and we're going to kill the ecosystem there. So not really a sustainable alternative unless we're aware of it, and then we plan accordingly as we implement it.

An effective life cycle assessment should be something that looks systemwide. So you'll hear the term cradle to grave. We ultimately want to look from the beginning to the end with the product life cycle. We want to think about multiple media: air, water, soil. We want to analyze multi-attributes. So we care about human health, but we also want to look at things like climate change and resource management.

If done correctly, I should be able to use an LCA to

identify tradeoffs among alternatives. So depending on what I'm interested in as a decision maker, there should be an option out there for me. I can identify opportunities for improvement in a single process, using things like hot spot analysis. And if I do all these things correctly, an effective life cycle assessment should lead to sound environmental decision making that can support sustainability.

You'll probably hear if you go through the literature, and this kind of ties into what we heard this morning, that there's the idea of standards. And so life cycle assessment is something that has been standardized at the international level, and ISO has within its 14000 series the 14040 and 14044 standards that describe the life cycle assessment framework. It's essentially a four-step process where we have the goal and scope definition, which is where we say what we're going to do, why we're going to do it. Then we get into our life cycle inventory, where we look at what's the type of data we need to do it. And then we try to understand what the impacts are by going through impact assessment. And, finally, we have this idea of interpretation, where we try to figure out what conclusions we can draw and how much we can trust them. And as you will see, these are two-way arrows. And so that means

that this is really an iterative process. All along the way as you go through, you always want to go back and revisit your goal and scope so that you can understand am I on the right path or do I need to readjust what I was thinking when I modeled the system.

The goal and scope definition is probably the most essential part of a life cycle because it's really where you state what's the purpose, why am I going to do this. Some of the purposes we're all used to seeing out there, the idea of product comparison. So if company A wants to say that its product is greener or better than company B's, and if you're a sustainably or conscious kind of consumer, you'll buy their product. These ideas are called comparative assertions, and it's fine as long as they follow the ISO guidelines, which require very stringent third-party review and certification of results.

We don't go there in the EPA. We more use life cycle assessments so we can look at maybe emerging technologies or sort of product systems of interest and get baselines for what are the environmental and human health consequences. We can then kind of communicate this information to other parts of the Agency, where people work with sustainable chemistry and

sustainable design principles. Then we can kind of communicate all of this to our policy development arena so that we can try to have some sort of an incentivized way to help industry get into a more sustainable tract. Some of the other ways you might see it as a consumer is this idea of ecolabeling that's becoming a big deal. It's typically driven by life cycle assessment.

A clearly defined goal will determine the scope of the study. Obviously, it sets the boundaries and scales, and I'll talk a little bit more about that in a second. And the key here is it identifies the product or process function. And that's really the big deal. When people talk about what's the difference between doing sort of the life cycle assessment and risk assessment, is life cycle assessment is a comparative look at a societal function, not necessarily the product itself. So, you know, the reason we're all here talking about e-cigarettes is not really that I would want to necessarily do a life cycle assessment. I mean, you could, looking at various types of e-cigarettes, but it's more that I understand there's right now a need in society for nicotine, some sort of a delivery of nicotine, and I want to compare and look at all the ways that a member of society could get their nicotine fix

with the least amount of impact.

And while I'm going through and setting this goal and scope, it helps me understand sort of what's the level of information that I need, what's the data quality I can trust, what sort of detail do I need. And if you don't do all this right and you don't get your functional unit right, in the end, you're kind of left with a comparison of the old apples and oranges.

I had said that there's this whole idea of scope and boundary, and so one of the big things that LCA has a strength of showing you is the idea of burden shifting. And so you will see two terms. People usually talk about cradle to grave or a gated life cycle assessment. We tend to stress people should do cradle to grave, and that's in the diagram. You have the giant red box around the entire product life cycle. If you look cradle to grave, this gives you a chance to understand that if I make changes in one part of the life cycle, it might affect and lead to more impacts in the other. And so if I do the gated system, which typically what you'll see is supply chain studies, yes, you might improve the manufacturing processes, but you might have done it at the expense of creating impact somewhere else in the life cycle

that negate the benefit.

Once I've established a goal and scope, it's all about the data. And this is probably the most time-intensive part of a life cycle assessment, and that's because essentially I'm trying to account for all the material and natural resource inputs and outputs in the product system. And so if I go and I talk to manufacturers at least for, like, the upstream, it's really you'll even find that they might only understand how they make their own material. If it's a precursor to a consumer product, they don't know what happens downstream or upstream of them, and so it requires you to spend a lot of time if you need the primary data of working up and down the supply chain and then across the life cycle in terms of waste management facilities and whatnot.

Data are usually presented in inventory at sort of a higher aggregated level. So everybody talks about there's all these models of vaporizers and e-cigarettes. And it might be that, you know, if you wanted to do policy development for an e-cigarette, you try to sort of create a market average inventory of all the different types of models as opposed to having to do a life cycle for each specific model, given the numbers.

In the end, this is the phase where you're going to see a lot of application of assumptions using the sort of rules of exclusion, what do I put in, what can I live without. And the point here is that it's understood in the life cycle community I'm going to have to make these assumptions, but I just need to be transparent about it and make sure they're communicated with the results.

Waiting on the computer. Hey, there we go. Life cycle impact assessment, big crazy diagram. But this is the one that I love to show because I think most people when you talk about all these broader impacts, everyone sort of tunes out after you say health impacts. When you start getting to climate change, when you start getting to resource depletion, people aren't necessarily sure, should I care, or why should I care, or what does that mean. But if you look at the impact assessment, it's really going from this idea of the inventory on the left, your SOx emissions, your NOx emissions, your total nitrogen emissions, your land use, things like that, and we go to this idea of midpoint categories. So this is sort of the first level of what I can understand as being the damage in the environment. And that might be human toxicity, but it might also be ozone depletion, climate change, ecotoxicity,

eutrophication, which was a big deal, you know, in Toledo a few months ago.

Essentially, I can then take these and translate these to endpoint categories, where I look at things like cancer, respiratory disease, infectious disease, land loss, user cost. I can then translate these even further downstream if I want into areas of protection, where I look at things like human health, ecological health, resource use. So, essentially, you know, when we get all these categories and we move to the endpoint, it's really getting back to an issue of health no matter if we think they're direct or indirect health effects. I should point out, though, the farther you go down towards this area of protection, the more uncertainty exists in the impact chain.

What do the results look like? It's just a simple bar graph, in most cases, where people will throw up alternatives and do this sort of comparative analysis. And the idea here is, you know, the bar is what the -- the smaller scores are your better alternatives. And if I were interpreting this, I would say that, you know, the red bars, obviously, is not a technology. In this case, these were television displays that we'd studied. You don't want to be using cathode ray tubes,

but when it's a choice between, like, field emission displays and liquid crystal displays, it really becomes a question of what's the uncertainty and how much can I trust the variations I'm seeing.

So in the end, that's the whole process, really, of conducting an LCA. And if you think about it, like any tool, there are the weaknesses and there are the strengths. For the weaknesses, it's really the fact that it's resource and time intensive up to this point. We're trying to work on things in our own research that can lead to having better data availability and help people, but it still takes a lot of time to go through and work the models and the assumptions. There's a lot of impact assessment models you can actually choose from depending on if you want European, North American, global, different types of impact categories. So it can be a little overwhelming for first-time users. It's difficult to assess emerging products and chemicals, and I think this is something that Hoshing touched upon in her talk. There's a lot of, like with e-cigarettes, unknowns, and so how do you treat that, not understanding necessarily the use patterns or how these things are necessarily manufactured at a large scale. And then, ultimately, there's always the potential of

people take your results out of context and they make bad decisions.

The strengths, though, is it is a holistic and comprehensive tool, and so we have this way to look at, you know, the full life cycle with an eye towards sustainability and use something that's very structured, well defined, it's, you know, internationally standardized. And in the end, it really kind of helps, we find, decision makers and stakeholders learn to communicate, because you have to talk through so many of the assumptions and the choices that go into a life cycle assessment.

So the last part of this, I really just want to take a second and talk about what does it mean for applying LCA to an e-cigarette. And this is not something my agency has thought about or looked at. It's just not really come up. But if I were given this task today or something, I kind of went through it like that, the first thing I would think and say in the goal and scope is I'm not even sure, necessarily, what are the right questions I'm trying to ask, because it seems very counterintuitive in this point that, for a lot of people, society is trying to say that nicotine use is wrong, and yet I'm now trying to find the most sustainable way to use

nicotine. So I guess it depends on who's doing the study and how you can sort of frame those questions, what side of the camp you find yourself in.

I want to look at, you know, if it's looking at the function of supplying nicotine, what are the types of environmental impacts I'm curious, you know, about, what all impacts do I want to look at, because that's going to help me decide whether or not I can look at a full life cycle or not. Am I going to understand the disposal issues so that I can include that phase of the product life cycle?

With the functional unit, this was a big one for me, is there's so much that you could go here. You could look at a single use, a year's worth of use, an actual -- the lifetime of a specific product. You could look at the nicotine requirements for a user in their lifetime and then how, you know, all the various ways that you can get this nicotine, how that changes the impacts. And then the key here that I heard yesterday that was coming up with me is what defines a dose of nicotine delivered. And so that's a pretty big question that it seems like we're not even sure necessarily, you know, what does the average smoker, what do they want in terms of the nicotine, or when do they feel right. So that's questions

that would have to be answered before you could even kind of get the functional unit out of the way.

And then the idea of what are we comparing. You know, earlier somebody was saying that we don't really want to benchmark, at least on the health side of things, versus traditional cigarettes. But from the environmental side, we'd probably want to just look at all the ways that we get this function. So we look at the vaporizers, the cigarettes, the -- what was they called it -- nicotine replacement technologies -- I'm learning. And the other issues was there seems to be a multitude of flavors. I'm wondering how all these flavors are produced and manufactured, but how would you cover all that realistically if they say there's like 1,000 flavors. You would probably spend your life trying to model all those in a life cycle assessment.

And, finally, there's the idea of spatial resolution. So is this something -- we only look at this from a U.S. context or do we look at this as being a global supply chain? In terms of the use, am I only interested in the indoor use scenarios? Am I caring about somebody walking down the street using this? Do I want to look at a combination of both? So what all plays into the spatial resolution?

For the inventory modeling phase, I can probably sum up all of these points and not take you through each of them by saying that it's really just -- where this is is kind of a newer arena to be thinking. Seems like there's not a lot of data out there, and so trying to understand things like use patterns, disposal patterns, the refill, the product useful life, how long you can keep a device before you have to replace it. It seems like there's a lot that would have to go into being able to run a life cycle assessment. And then in the end, am I still going to have data gaps and are they gaps that I feel I can live with in terms of my decision?

In the impact assessment phase, there's the impact category selection, what impact should be included. And I was thinking about it. This is probably, from a regulatory side or at least a policy development side in the government, this is an interesting question because I think it really depends on what agency you are in terms of which impacts tend to stick the most, because I'm thinking in my mind, like, if FDA wanted to run a life cycle assessment, are they that interested in land use impacts during the tobacco farming phase, do they have that sort of power to influence the land use associated with tobacco growth, or is it something where then they need

to look at sort of making this interagency, where they bring in other parts of the federal government to look at this type of a study?

Putting those questions aside, once I get into the impact methodology, like I said, there's tons of choices out there. Is there, you know, appropriate methods for all the impacts I'm interested in? Are the chemicals represented in it? So I can have a method, run the life cycle assessment, and get a bunch of zeros just because there are no what they call characterization factors that actually tell me what the impact associated with that chemical is. And so I think with all these sort of new additives, new flavors, you would have a challenge developing the characterization factors, which are usually based on things like LD50 values and some -- transport parameters.

And, finally, are all relevant impact pathways captured? So one thing I couldn't get into in this sort of shorter timeframe of this is that traditional life cycle assessment has been a far afield exposure tool. And so for people who don't know what that means, it means we've looked at a company is manufacturing a chemical somewhere at a plant, it goes -- you know, a chemical is emitted out of the stack, how does

that impact us in terms of going through all the environmental media coming in through the food chain. But recently people in the life cycle community realized that, you know, probably orders of magnitude more important is this idea of consumer product exposures. And so there's a lot of work right now that, although it's not currently, it's anticipated in the next year or two this'll be part of the methods, but being able to look at if I'm that person using this vaping device, what does that mean for me, what does it mean for the people around me when I exhale, if things deposit on surfaces and someone comes along and touches the surfaces, what does that mean? So this is very much a different type of exposure science than what has been used traditionally in life cycle assessment.

And the final thought I always like to lay out is even if you're going to do some sort of an environmental impact assessment, that should really be just one part of your decision. And so, really, you have to think about this in terms of if I come up with alternatives that are better environmentally, are they technically feasible, are the costs realistic, you know? If you're thinking in terms of sustainability, there's the economic considerations. You

can't go bankrupt in industry overnight, because those people employ people, and so that's, you know, it's part of the economic sustainability of something. So we have to find ways that we work through the various aspects of these decision tools to find a path forward that works for everyone.

And so really, just to summarize, life cycle assessment is a standardized method to evaluate product impacts across their life cycle. It's holistic. We look, you know, all across the life cycle so we can understand things like tradeoffs and burden shifting, try to avoid the unintended consequences. Life cycle impact assessment will only be as good as the information that you can feed into it. So that's really kind of understanding your uncertainty and the assumptions. And then, finally, LCA is only one piece of the puzzle when we make decisions.

And that was really all I had. So thank you everyone for listening late in the day on the second day.

(Applause.)

DR. DRESLER: Okay. Our next speaker is also from the Environmental Protection Agency. Kristin Fitzgerald will be speaking on the Disposal of E-cigarettes.

MS. FITZGERALD: We're going to bring the mike back down.

Hi, I'm Kristin Fitzgerald. I'm also from EPA, but I'm from a very different part of EPA than David works at and a very different kind of perspective than many of you in the room probably have. I have nothing to do with the development of products or regulation of products. I work on waste. So I work in a part of the agency that deals specifically with hazardous waste. And although I have at one stage of my career worked in laboratories conducting research, I've spent the bulk of my career working on writing and interpreting hazardous waste regulations.

So that set of regulations is called the Resource Conservation and Recovery Act, or we call it RCRA for short. So quick show of hands. Anybody even heard of RCRA in this room? Oh, that's way better than I was expecting. All right. Good. All right. So for those that didn't raise your hand -- I was expecting, like, maybe one hand, tops, so that's a big surprise.

Okay. So for those of you who didn't raise your hand, you've probably heard of Superfund, which, you know, helps clean up historical waste sites. RCRA is kind of the sister program with Superfund, where we're charged with -- you know, it's a preventative program, manage hazardous waste from

cradle to grave properly so that you don't end up creating these waste sites in the long run.

So my goal here is not to turn you all into RCRA experts. I've seen, you know, 25 years working on RCRA, and there's still aspects that I don't actually understand. But just to kind of give you a quick introduction so that you're aware of RCRA and that it may apply to certain disposal scenarios for e-cigarettes and the e-juices.

I will give you a quick disclaimer. I have no financial disclaimers. Federal government, no funding. I am only speaking about federal regulations, okay? States and localities may have additional regulations that can be more stringent than the federal government. So I'm only talking about the federal program.

Just a quick outline of what I'm going to be talking about. What we've been doing to learn about e-cigarettes, share what we've learned so far, which is not as much as I would like. I've learned a lot in the past couple of days. And talk about disposal both by consumers and by nonconsumers, because RCRA handles those very differently.

So over the past year or so, we've been in learning mode about e-cigarettes as they've come onto our radar screen, and

people start asking us questions primarily from manufacturers, you know, and retailers, and what do we have to -- what are we going to do when we have to dispose of these things. So you know, some of the questions we've been asking is what types of cigarettes are on -- e-cigarettes are on the market, what are they made out of, and are any of those contents potentially hazardous waste? So we're in very much information-gathering mode so that we can make some informed decisions about how the e-cigarettes need to be disposed of either by the consumers or the non-consumers, manufacturers, retailers, and so on.

So I've broken the e-cigarettes down into three general categories. And I know people have kind of put them into different categories, but for my purposes, I find this useful. One is kind of I think what people have been referring to as the one and done, you know, disposable. They're one piece; they're prefilled. You're going to use it till it's done, and then you're going to throw it away. And these are primarily found at retail stores. They only hold about a milliliter of the nicotine e-liquid.

The second is the one I've probably seen the most is the usually two-piece. They usually come with a rechargeable battery, and you know, they kind of screw apart, and there's

the battery end, and then there's the prefilled replacement nicotine cartridges. And those little cartridges hold, again, about maybe a milliliter of the nicotine solution. And, again, these are primarily found at nicotine -- excuse me -- retail stores.

And then there's kind of the refillable types. And these are the ones that seem to have the most variation. So you know, whether they're two-piece or rechargeable seems to vary a lot, but they have refillable nicotine cartridges or reservoirs. You're going to find these more at your vaping stores, and you can refill them on your own or you can have them kind of made for you, custom made for you at the vaping store. And then there's the -- these tend to hold sometimes more nicotine than the others. But as we've heard from Dr. Quinlan's presentation earlier, there's the containers of the e-liquid, and those can come in small vials to large containers. I've seen, you know, gallon containers advertised online, you know, sometimes even 55-gallon containers you can buy online.

So common diagram everybody keeps putting up over the past couple of days. I think I can gloss over this. And the contents that, you know, are primarily involved and the

e-liquids, the nicotine is varying in concentrations, kind of the -- you know, as high as 10%, I've seen on the market. Although from what I gather, there is no regulatory limit to what the concentration can be, that's the highest I've seen for sale. But the lower concentrations, from maybe 2 to 3% seem to be more typical on the market. Also -- over the past couple of days, I think I can skip over the e-liquid contents. The other contents -- these slides, by the way, are based on information that manufacturers have submitted to us primarily. And, you know, it's come up the past couple of days it varies a lot from the type of e-cigarette, and as soon as we think we know what the heck they're made out of, then it changes, and it's a different thing. But they do tend to mostly have a few things that we're concerned about.

Lithium batteries and liquid nicotine seem to be the two components that, from our perspective, hazardous waste disposal are the most problematic. And I will say that I did look at the propylene glycol and the polyethylene glycol to try and figure out whether they might be hazardous waste. We have a category of hazardous waste that are called ignitable. D001 is the waste code that's associated with that. And if liquid has a flashpoint of below 60 degrees centigrade, then

it would be ignitable in our regulations. And both propylene glycol and polyethylene glycol flash above 60 degrees centigrade. So I think we can rule those out as hazardous waste.

Let's talk about the lithium batteries and the e-juices. The lithium batteries, my takeaway message is we're still learning. And if anybody has information about them, we'd be happy to have it. I know there's another presentation or was one this morning about batteries, and he's going to be talking again in a little while. And we are definitely in need of expertise about lithium batteries. We're still gathering information about them. Our biggest concern is whether they would be considered reactive under our regulations. That would be a D003 hazardous waste code. Reactive can -- there's a number of different ways something can be considered reactive hazardous waste, but probably the one that we're worried about here is things exploding. And as the presentation this morning suggested, lithium batteries and consumer electronics can sometimes explode.

So our current understanding, however, is -- and this is based on very limited information, so we're open to learning more about this -- that the batteries in e-cigarettes are

probably unlikely to exhibit the characteristic of reactivity because, one, even if they're fully charged, they're relatively low voltage, at least as originally manufactured. And I know people tinker with things and can change things, but at least as originally manufactured, they tend to be low voltage and probably would not exhibit the characteristic of reactivity. But presumably, when they are disposed, which is when the hazardous waste regulations would kick in, they would be discharged. I mean, that's why they're probably disposing of them because the battery is not working anymore. And when they're discharged, they would be much less likely to exhibit the characteristic of reactivity.

One of our questions, however, is, okay, the battery is dead, I'm going to throw it away as a consumer; now what do I do with it? They are theoretically recyclable, the batteries, but they're not easily accessible. It's not like you can just take it out of, you know, your little toy or something. You got to -- there's some disassembling that has to occur. So that makes the recycling for consumers rather difficult. So it's not clear to us whether any battery recycling from consumer e-cigarettes is actually occurring at this point even though it is theoretically possible.

Okay. Now let's talk about the nicotine. Since 1980, when the first RCRA regulations were promulgated, product formulations of nicotine, when they're disposed, have been considered to be acute hazardous waste based on its acute toxicity. Now, I wasn't going to get into this, but it seems like this audience is more than ready to deal with talking about the toxicity that's incorporated into the regulations, kind of the standards for the toxicity incorporated into the regulations. The criteria are, in some respects, rather vague, but in other respects very specific for whether something is acute hazardous waste. The regulations say, one, if it's fatal to humans in low doses or, in the absence of human data, as an oral rat LD50 of less than 50 mg/kg, an inhalation rat LD50 of less than 2 mg/L, or a dermal rabbit LD50 of less than 200 mg/kg. Or if, in the absence of all that, otherwise capable of causing or significantly contributing an increase in serious, irreversible, or incapacitating reversible illness.

So back in 1980 or actually '78 is when we proposed the regulations, we based our decision for acute toxicity on oral human data as well as dermal rabbit. The oral human data was estimated. Now, at the time, there were no e-cigarettes.

There was no nicotine replacement therapies. Nicotine was primarily used in very high concentrations as a pesticide. Now, certainly, e-cigarette manufacturers start with those high concentrations, but then they, you know, dilute them down for use in e-cigarettes. And I think one can assume that lower concentrations of the nicotine would have lower toxicity. However, as Dr. Quinlan very strongly pointed out this morning, there still are very strong concerns about the toxicity of nicotine even at the lower concentrations, especially in children, and that's something that we have to consider. Although adults are obviously the intended audience, they are not the only people ingesting these things.

So we currently lack sufficient data to make any kind of cutoff to say that, well, at this concentration, nicotine would be considered acutely hazardous waste, but at this concentration, we can say it's just regular hazardous waste. And on the slide, it says toxic versus nontoxic, and I really shouldn't have worded it that way. It should say we don't really have a concentration cutoff where we can say, okay, this is acutely toxic and this is not acutely toxic. So, therefore, in the absence of that data, all nicotine formulations regardless of concentration are considered acute

hazardous waste when they're disposed. And that includes the e-liquids, that includes gums, lozenges, patches, and, you know, so -- and due to what I consider a bit of a loophole in our regulations, it only applies to unused products. E-liquids are only going to be disposed of when they're unused anyway; otherwise -- presumably.

We are actively seeking additional toxicity information for nicotine at low concentrations, for example, you know, LD50 information, so that perhaps we could make some kind of distinction for a low versus high concentration of whether something is acutely toxic. That information would probably play more into a decision about gums, lozenges, and patches than it would for e-liquids. But if anybody has information that they're aware of, we'd be happy to have it. As Dr. Quinlan pointed out earlier, although nicotine has been studied for years and has existed for years in all kinds of products, the LD50 is rather difficult to obtain. Let's say an LD50 that everybody agrees on is rather difficult to obtain.

So now having said that nicotine in e-liquids is a hazardous waste, not everyone who disposes of it is regulated. Okay. Residential disposal versus nonresidential disposal are

treated very differently. Disposal of the e-cigarettes along kind of with normal household trash at residences is not regulated by EPA. It's what we call household hazardous waste. And it's not necessarily a judgment about whether or not it's toxic. It's more kind of a practical matter. Congress said, well, it's not very practical to regulate every household's disposal of waste, and therefore, it's not regulated disposal.

Let me put a couple of comments in here. One is that if you are manufacturing in your household, and I hear that that is happening sometimes, that's not normal household trash, and that would not be considered exempt as household hazardous waste. That would actually be regulated waste. My other thing is that we have had a longstanding recommendation that even if it's not regulated, we would recommend that you recycle -- or excuse me -- hand in your household hazardous waste to a household hazardous waste collection program. But here's my question. We need information about whether household hazardous waste collection programs are accepting e-cigarettes, and if so, what are they doing with them? Are they able to recycle the batteries or are they simply just being disposed?

Nonresidential disposal, and I know my time is up. This is my last slide. This goes for basically everybody else. We're talking labs, researchers, universities, manufacturers, retailers, federal agencies, healthcare facilities, anybody else who is disposing of these e-liquids, you are disposing of hazardous waste. And even in very small quantities, meaning more than 1 kg per month, you are fully regulated as a hazardous waste generator. We call them large quantity generators, so that means you're fully regulated because it's an acute hazardous waste. You're regulated more fully at very low quantities. For example, FDA facility lab has -- you know, we're 600 acres, I think, this facility -- almost certainly is a large-quantity generator. It's not on a lab by lab basis that you determine the 1 kg per month. It's for your whole site.

So the e-liquids are very clearly P-listed acute hazardous waste. We're still evaluating, however, whether the e-cigarettes themselves would be classified as hazardous waste under RCRA. And just my contact information if anybody has follow-up questions or information about battery recycling or toxicity of nicotine would be welcome.

(Applause.)

DR. DRESLER: Okay. We'll do the panel. And so I will ask the speakers of the panel, and also Dr. Sarkar from Altria Client Services will be joining the panel. So if we can have the people come forward?

So, Dr. Sarkar, I just said your name, but did you want to introduce yourself at all? Or -- no?

DR. SARKAR: Good afternoon, everybody. My name is Mohamadi Sarkar. I am a Senior Principal Scientist in Regulatory Affairs at Altria Client Services, and I am participating in this panel on behalf of NuMark, which is an Altria company. And thank very much, CTP, for inviting me to contribute in this panel.

DR. DRESLER: Okay. All right. So if you have questions, same thing, write them and get them to the corner, or to the sides.

Does EPA work with state and local governments in terms of collecting household hazardous waste? So I'm not sure you collect the waste itself, but does EPA work with state and local governments, I guess, on the regulation of household waste --

MS. FITZGERALD: Right. So we have recommendations for how household hazardous waste is collected, but it's usually

done by municipalities, counties, and so on, the actual collection. We have recommendation that household hazardous waste, once it's collected, be managed as hazardous waste, because if you're just going to turn around and manage it as non-hazardous waste, what's the point of collecting it, because people could have just put it in their trash at home and saved a lot of gas bringing it to the household hazardous waste collection program. So we have a longstanding recommendation to household hazardous waste collection programs to manage that waste as hazardous waste if they go to the trouble of collecting it. And I think most do.

DR. DRESLER: Okay. Some flavoring compounds have a flashpoint less than 60 degrees. How does EPA assess the flashpoint of finished e-liquids?

MS. FITZGERALD: We haven't addressed the flashpoint of finished e-liquids. And it's actually the way the regulations work. It's not our responsibility to. It's the generator's responsibility to determine whether or not they have a hazardous waste. But that's good information to know, that the flavors do flash below 60, and if you throw those flavors away independently, if, you know, it's off spec, it's not a popular flavor, whatever, and it flashes below 60, that's part

of your hazardous waste stream then. Once it's incorporated into the product, the finished product would have to flash below 60 to actually be considered a hazardous waste for D001, although the e-liquid is already a hazardous waste because of the nicotine. Additional characteristics are important, but it's already a hazardous waste.

DR. DRESLER: Okay. All right. So can the panel discuss, please, what are the key components of a battery recycling program?

DR. SARKAR: So let me tell you something about our program. You know, at Altria, we consider the whole concept of environmental sustainability is important, and it's part of our mission goal. So we're committed to minimizing our environmental footprint. Now, as far as NuMark's products are concerned, you know, we sell MarkTen, as you heard earlier. And MarkTen is made up of kind of a rechargeable e-vapor product, and it consists of both a cartridge and a battery. And the battery recycling we do through three ways by which consumers can get this information: One, we actually have a product insert in the package, which gives the consumers information about how to dispose of the batteries; second, we have information on the website; and third is that they can

call the toll-free number. And essentially, rather than having a slide, I thought I'd bring a show and tell.

So we actually, when consumers call us, we send them a prepaid envelope in which they can ship to us a postage-paid envelope. They ship the cartridges, because the two components of the e-cigarettes that are of concern for potential environmental impact are the cartridges and the batteries. So they can send the cartridges in this, and then we also have another envelope in which they can send the batteries. And the batteries are included in this along with the cartridges and mailed; then they are recycled. We also actually partner with a third-party vendor, which has drop-off locations that are conveniently located in grocery stores and your local hardware store or in the office supply stores, where they can drop off the batteries. So a lot of it, of course, depends on how engaged the consumers are in participating in the recycling program, but we do offer lots of resources for them to choose from.

DR. MEYER: I guess I can add to this just from my perspective. And when we think about recycling and life cycle assessment, and we look at certain product systems -- I just did a study last year on rare earth elements, so not quite

lithium, but the same companies that would look at doing, like, lithium-ion batteries, in general, from cars and other electronics, they were, you know, considering rare earths, and it seems that when you talk to a lot of these companies, part of it's not just having the infrastructure to get the consumers to put it out, but you have to look at the actual recycling process. Is it something that, compared to say, you know, a manufacturer using primary materials coming out of the mine versus these secondary materials, does it make sense? So unless you have like a closed loop, a company takes it back themselves, just in general, turning over your batteries, it really is -- it's a volatile -- you know, it depends on the market, I guess, for the metals. And that's at least been some of the issue with some of the less precious metals is, is there enough of a product market that somebody that's going to recycle can actually do that.

So there's some incentivizing that has to be done sort of on the, I think, on the recycling industry part of it. And that's where another part of the Office of Solid Waste that we work with and the Sustainable Materials Management people, that's what they sort of engage and try to work with some of these sort of metals recyclers and what they can do to sort of

help propel that.

MS. FITZGERALD: Yeah, I would mostly have a question, I guess. One of the things that we've noticed is that -- spent lead acid batteries, the kind of batteries you have in your car, are widely recycled. I think, you know, something like 90% are recycled for the lead primarily. But we don't know. I think the lithium batteries are relatively new in the, you know, in the kind of waste market, and I don't know to what extent lithium batteries are being recycled at this stage. And if they are being recycled, I mean, there's a vast array of lithium batteries. Which ones are more likely to be recycled, and you know, what size and what type of lithium batteries?

DR. DRESLER: Just to sort of follow up on that, are they being used? I mean, you've provided a prepaid envelope and everything, so are the consumers recycling them? How well is that going?

DR. SARKAR: Well, yes, the short answer to your question is yes. We are getting calls from consumers, and it is being used. But, of course, you realize that we just nationally launched our product, and this is kind of a new and evolving space. And hopefully as the awareness grows, perhaps more

consumers will then participate on this.

DR. DRESLER: Okay. All right. Ms. Fitzgerald, are there disposal instructions for other products under EPA's jurisdiction that could potentially be relevant to those of e-cigarettes? So disposable [sic] instructions that you would recommend? Are there disposal instructions for other products under EPA's jurisdiction which could potentially be relevant to those of e-cigarettes? So do you provide this? I think what this question is asking do you have disposal instructions, would you have recommendations, or is that something maybe the manufacturers would be doing?

MS. FITZGERALD: I guess for the consumer would be different from the regulated folks, right, so --

DR. DRESLER: And think this was going for the consumer, how this question was --

MS. FITZGERALD: Right. So for consumers, I mean, generally we advocate household hazardous waste collection, but here's the problem, is that since we don't actually run any of the collection programs ourselves, we don't control what's accepted. So, you know, that's something I want to look into. I've looked into some of the local jurisdictions around me, and they have a list on their websites of the

things that they accept. So far, they don't say on their websites that they're accepting e-cigarettes. I don't know if that means that they won't accept them if you bring them, but I think it's still new, and it will evolve, and I suspect that household hazardous waste collection programs will come to take them. And that's what I would recommend.

DR. DRESLER: Okay. Thank you.

With regard to life cycle analysis, what is known about the reduction in need for tobacco if e-cigarettes replace cigarettes? So e-cigarettes deliver nicotine more efficiently, so less is needed.

DR. MEYER: Yeah, so that was actually my question when I had conversations with some of the researchers at FDA, was probably you would be looking more at sort of what they call a consequential analysis. And I honestly don't have the answers to this. But it is a question of -- and some people were trying to explain to me yesterday that it all has to do with the efficiency of the nicotine, so that if someone smokes combustible nicotine, apparently it's a lot less efficient. So you would, in theory, think if everyone converted over to sort of an e-cigarette, you would reduce the need for the amount of tobacco grown because you could extract and use that

same amount of nicotine more efficiently. But, again, I've never done the assessment, and I don't have the numbers. But that is a question that I would have probably designed a study to look at if I were doing this in life cycle assessment.

MS. FITZGERALD: I might just add to that. I know nothing about life cycle assessment, but one thing that might impact the need for tobacco as a source of nicotine is that I know at least one company is now taking nicotine products, patches, gums, lozenges, e-cigarettes, and extracting the nicotine and recycling it and then selling it to a purifier who then gets it up to pharmaceutical grade, all right? So they're taking nicotine that's already been extracted and re-extracting it and reusing it.

DR. DRESLER: I think that follows up because one of the questions: Can nicotine liquids be recycled rather than disposed of as waste? So --

MS. FITZGERALD: Right, I do know of this one company that's just getting off the ground to do recycling of nicotine.

DR. DRESLER: Nicotine replacement products?

MS. FITZGERALD: Right, right, and from e-cigarettes. I don't know if they're -- I know that their plan is to accept

e-cigarettes from retail stores. I don't know if they're planning to accept e-cigarettes from consumers.

DR. DRESLER: Okay. Dr. Sarkar, after you collect the used e-cigarettes, how do you process them, landfills reclaim them, so what do you do with the e-cigarettes and the batteries when you have them?

DR. SARKAR: Sure. So, as I said, you know, the two components that are important are the lithium batteries, the rechargeable batteries, and the cartridges. So the lithium-ion batteries are recycled, and the cartridges are incinerated.

DR. DRESLER: Okay. What is the current policy of the EPA on disposal of small electronics that contain lithium batteries? Would you expect anything different for e-cigarettes? So how is the EPA -- if small electronics contain lithium batteries, then what's that current policy for EPA, and what would you expect different for e-cigarettes?

MS. FITZGERALD: I think my answer is going to be I don't know. It's a little out of my expertise.

DR. MEYER: And if she doesn't know from the Office of Solid Waste, I definitely don't in our Office of Research and Development.

DR. DRESLER: Okay. Okay. So when market volume projection is available, could life cycle analysis include that factor into the analysis? So if you know the market volume of what's being sold, can you use life cycle analysis -- can you use that market volume projection in your life cycle analysis?

DR. MEYER: I guess the question I would have is in what context do want to use it in your analysis. You can always use market-driven projections. You can even look at shifts in the market. So if you understand the product size, then you make, you know, future kind of scenario analyses where you're looking at if less people stop using or more people, what does that do to the resulting impacts for the sector. You can use that as a basis for defining your functional unit. You can say I have a market that I need this much nicotine. What's the best way of supplying that via -- through the vaping or the combustion or the replacement? So, yeah, if that information became available, you can always find ways to include that in some sort of a life cycle assessment.

DR. DRESLER: Yes?

DR. SARKAR: This is just a comment, you know. We saw in the past presentations that the types of e-vapor products are

such a wide range. So one life cycle -- and this is more of a question for Dr. Meyers [sic] -- is that one life cycle assessment for a specific category of product, let's say the rechargeable cigalike products, I don't know whether they would apply to a tank type of product. And the whole e-vapor category is so disparate, and there's such a wide range of products that it's going to be a challenging task at hand.

DR. MEYER: And so I guess that goes to what I was saying you would have to start in levels. You would have to look at if I take two kind of prevalent types of technologies, and unfortunately, I don't really know much about e-cigarettes to tell you, but so if you took two of the prevalent, like the cartridge versus the tank or something, and compared those, and you found that the impacts are really essentially the same from, you know, that it's about the same types of materials go into making it, then you kind of build your scenario that way of can I use an industry average or do I have to have sort of product class specific. And that's really just a question of who's making the decisions and what questions they're asking. But yeah, you're right. I mean, with the variability, you can do something that's crude and sort of just an approximation of e-cigarettes in general, or you can have very specific for

specific classes of devices.

DR. DRESLER: Okay. So, Dr. Meyer, can life cycle analysis include the global warming effects of the environmental impacts of e-cigarettes?

DR. MEYER: So, in general, most life cycle assessments -- I think, in fact, most people when they say they're going to an LCA, they wind up doing what we typically call a carbon footprint or some sort of greenhouse gas emissions. But you have to understand that the numbers you get, it can include, if you want -- if I know the emissions, say, of a, you know, vaping or whatever, what's coming out, if I feel like there's constituents in there that play into the greenhouse gases, yeah, I mean, that can be characterized as part of your inventory. But essentially you're looking at all of the greenhouse gas emissions associated with, you know, the entire life cycle. So, yeah, that's obviously one impact category people tend to look at just given all the push for the climate change internationally.

DR. DRESLER: Which of the following creates the most waste or the worst waste: used cartridges, used liquid bottles, or disposable e-cigarettes? So your choice between door one, two, or three: used cartridges, used liquid bottles,

disposable e-cigarettes. Which -- is there a worst one? How do you evaluate that? Hard choice, yes.

DR. MEYER: I'm just going to play a guess here. I mean, there obviously -- you know, we'd have to do a lot of actual assessments to answer this, but if given the choice, the question I would have is when you talk about a disposable e-cigarette, does that include all of the electronic components that go into it, or is that, like, is that a disposable e-cigarettes, are they vaporized, I guess, electronically?

DR. DRESLER: So I'm going to make this up from the question, okay? So that's going to include the electronics.

DR. MEYER: So in my mind, I would think from disposing -- I guess the question you're looking at is if I just have the cartridge and you're worried about sort of the residual solution. I mean, first, it depends on whether or not that gets classified as a waste, like a hazardous waste. Number two is the disposable. What was the third option?

DR. DRESLER: Used cartridges or used liquid bottles or the disposable e-cigarettes that have the electronics in them.

DR. MEYER: So in my mind, I still think I want to go to the -- kind of complete product, because I think you bring in

more when you talk about some of the metals and whatnot that go into circuitry. I know other people are going to push back that it could be that you have the leach in the landfills from, you know, the bottles or something like that, but I think for me, I would probably go with the complete -- the sort of disposable product, because it sounds like it has more of all the entirety of the guts in it. So that's just my opinion.

DR. DRESLER: Any other comments?

MS. FITZGERALD: Yeah. I mean, I guess it just depends upon the perspective of why you're asking, too. I mean, if you're looking at it from an exposure standpoint, if you've got an empty or relatively empty e-liquid bottle floating around your house, that's a much more likely pathway to exposure than an empty cartridge, right? If you've got kids and you're worried about them getting poisoned, right, an empty cartridge would be much harder for them to get the e-liquid out of than an empty e-liquid, you know, bottle.

DR. DRESLER: Okay. Sort of following up on that, are there ways to reduce the environmental waste and pollution from e-cigarettes? So we just went through which one is worse, which is a hard question, but are there ways to reduce

the environmental waste and pollution from e-cigarettes?

MS. FITZGERALD: Well, I mean, to the extent that you can use ones that can be reused, right? I mean, if you have the two-piece one where you're just throwing away the cartridge every time, that's probably better than doing the one and done, right? But this is a very narrow kind of non-life cycle assessment analysis, right, that as far as the amount of waste that you're throwing away, it's, you know, the more reusable components you have I would think would be the better.

DR. MEYER: I mean, essentially, I would say you would have to run sort of a baseline assessment, and then you would have to have companies that are willing to work with those impact results, so undergo sort of new product design, because that might mean tweaking the materials that we use in them. It might mean we change the sort of -- the electronics that are required so that we get the sort of delivery we want. I mean, there's always a lot of options you can do. You know, even when it comes to the toxic compounds, I work with people, you know, sustainable chemists that will tell you, you know, it's their dream in life that you show them a toxic compound and they'll design an alternative that's not toxic anymore. So I think you can always improve upon the impacts, be that

environmental or whatnot, of these products, but you have to have some sort of a basis to understand what you're changing instead of us sitting here saying we can change this or that, because I've never seen what the actual impacts are of these devices.

DR. SARKAR: I'm just making a general comment. I think that what we'll see is that there is so much innovation and there's so much technology that's going into the making of these products, who knows, maybe 2, 5 years from now, the products will be sustainable in a way that, you know, that this is beyond the comprehension of what we are looking at this product today. So perhaps it is possible. And as more and more innovation will come into this category, we will see improvements in that space as well.

DR. DRESLER: So am I hearing that we should think about what those environmental impacts are as -- moving forward.

Okay. So coils are being refurbished at some vape shops. Has a TCLP for chromium been done on the waste metals? So coils are being refurbished at some vape shops. TCLP -- and that's an alphabet soup. I'm sorry. I'm not --

MS. FITZGERALD: TCLP stands for toxicity characteristic leaching procedure. So --

DR. DRESLER: Of course, I'm sorry.

MS. FITZGERALD: -- that's one way of testing whether something is a hazardous waste for -- there's two ways things can be a hazardous waste. Either it's a listed hazardous waste or it can be a characteristic hazardous waste. And there are four characteristics, one of which is toxicity. And when we determine if something is a toxic characteristic waste using the TCLP, there's only about 24 constituents that one would test for, chromium being one of them.

No, I don't know that anybody has done the TCLP. I would caution against refurbishing them in a setting like that, because the chromium is probably contaminated with nicotine.

DR. DRESLER: And why is that a problem?

MS. FITZGERALD: Right. Well, one can only treat -- so that would be considered treatment of hazardous waste, and one can only treat hazardous waste under certain conditions, and usually that requires a permit. So I would caution somebody doing that.

DR. DRESLER: Okay.

MS. FITZGERALD: But I don't know if the chromium wire would fail the TCLP. I don't know how, you know, what other constituents are used in the coils other than chromium.

DR. DRESLER: Okay. So what are the environmental impacts associated with obtaining nicotine for e-cigarettes on an industrial scale? So getting a nicotine on an industrial scale to make the e-cigarette or the e-juice, what are those environmental impacts?

DR. MEYER: This might be another collaborative answer. I am not very familiar with the entire manufacturing process, but I can say, in general, talking about an agricultural plant first that we extract from, so in growing the plant, it would be sort of whatever water use goes into that, the land use, if we use any sort of pesticides, fertilizers. I'm not exactly sure how they extract the nicotine, but depending on what the extracting solutions are, that can require some sort of downstream wastewater treatment. And this is where I said I'm just thinking off the top of my head here. And I don't know what other kind of solid waste can be generated from the leftover parts after you've extracted the nicotine and where that goes, whether that can obviously lead to some other issues. But this is where someone that maybe knows the manufacturing process can help us.

DR. SARKAR: Well, I'm afraid I don't know the full manufacturing process, but I think you raised some important

considerations. And just to add to that, you know, the whole agricultural process of growing tobacco and then processing the tobacco and transporting the tobacco and all of the environmental issues that are associated with all these different processes would need to be taken into consideration, so the short answer to the question is that it really depends. And one would have to look at the whole comprehensive landscape before you can make that determination.

DR. DRESLER: Okay. Cigarette butts are the most littered product. Does the elimination of waste figure into a LCA?

DR. MEYER: So, yeah, actually, if you were comparing, you know, alternative functions of getting your nicotine, in the one case, if you're using a combustible cigarette, you would have a waste that consists of the -- if people are throwing out the butt, and it would have to go, you know, somewhere into a treatment. And I guess you wouldn't have that same material flow in your alternative of like an e-cigarette. So in theory, yes, you should see the difference between having sort of the physical throwing down your butts or the, you know, whatever the disposing of the vaping products.

DR. DRESLER: Okay. All right. Any other questions? We've been through our questions. Do you guys have questions

for each other?

(No response.)

DR. DRESLER: No? All right. Thank you so very much for the panel.

(Applause.)

DR. DRESLER: So we have one more session to go, and this last topic for this afternoon is environmental considerations -- no -- do you know what? Wrong one. That's what -- I have too many things in my hand. Sorry about that. Pull up the correct one, since we just did that. Thank you. But it is still the last one. Considerations for Chemical Constituent and Hazard Labeling.

And our first speaker is Dr. Betsy Scroggs from the Center for Drug Evaluation and Research at the FDA, and she will be speaking on Over-the-Counter Drug Product Labeling in the United States: The Drug Facts Label.

DR. SCROGGS: Okay. Hello, everybody. Thanks for hanging in there to listen to this talk at this session. We have a couple more after this.

I don't have any financial disclosures or otherwise to communicate with you. However, I will disclose that, as far as the alphabet soup and acronyms we like to use at FDA. So

we can communicate with each other, I'll try to define those before I roll into using those.

I am Betsy Scroggs. I'm the Acting Associate Director for Labeling in CDER's Division of Nonprescription Drug Products, or DNDP. There's your first acronym. Nonprescription drug products are those drug products that are available to consumers without a prescription. Nonprescription drug products is another way of saying over the counter, or OTC, as we probably all commonly refer to those. As with prescription drugs, CDER oversees OTC drugs to ensure that they are properly labeled for consumers and that their benefits outweigh their risks. I'm going to take just a moment to adjust this because I'm a little bit taller. Okay. Thanks.

Okay. So DNDP is CDER's group primarily responsible for this OTC drug product activity. However, scientists and regulators throughout CDER, the Office of General Counsel, and other centers within CDER -- within FDA, such as the Center for Tobacco Products and CDRH, are routinely asked to assist us in our review efforts. Very relevant to the topic of this workshop, I should mention that DNDP manages the review and labeling of the OTC nicotine replacement drug products used for nicotine cessation.

We conduct this review of OTC nicotine replacement drug products mainly in collaboration with CDER's Division of Anesthesia, Analgesia, and Addiction Products. Let's see. I go down. You know, I've never used this before.

DR. DRESLER: Use this --

DR. SCROGGS: All right. Thanks. Good.

All right. So what I'm going to try to talk to you about today is to introduce the Drug Facts label. I'm going to describe the OTC drug product labeling requirements. I'm going to give you a little Drug Facts label history as to how the Drug Facts label came into existence. I'll also give you an overview of the Drug Facts label content format, what that looks like. And last but not least, a few references that you may find helpful.

So this image may resonate with you as it does with me. A consumer views a shelf filled with a dizzying array of OTC products. So many choices. How do we and other consumers make a reasonable choice? We know that whenever we use an over-the-counter medicine, reading the drug product's labeling is important for taking care of ourselves and our families. The label tells us that what the medicine is supposed to do, who should or should not take it, and how to use it. The

labeling of OTC medicines has always contained usage and safety information for consumers, but it has not always been uniform and easy to read.

OTC drugs play an increasingly vital role in America's healthcare system by providing easy access to certain drugs that can be used safely without the help of a healthcare professional. This enables consumers to take control of their own healthcare in many situations. There are more than 100,000 OTC drug products marketed in the United States encompassing about 800 active ingredients.

Starting in the early 1990s, consumers complained to the FDA that they needed a better way to be able to understand how to make choices and use the OTC medicines that were available to them at the time. Previously, information about product directions, warnings, and approved uses appeared in different places on a label depending on the OTC product and the brand of that product. For those of us with allergy concerns, finding information about inactive ingredients had also been a challenge for those who may be allergic to an ingredient in a drug product. So what did we do? So in response to these concerns about the readability of OTC drug product labeling, in 1999 FDA introduced the Drug Facts label with OTC drug

information that is more uniform and easier to read and understand.

Next, I'll provide a little bit background on how the Drug Facts label was developed and what information it provides to the consumer. But, first, I need to tell you about a key definition here. We call it the Drug Facts label, and I have emphasis on label. The definition of the word "label," as defined under the Food, Drug and Cosmetic Act, is key to our work at FDA. What is a label and what is labeling? The term "label" is defined under the Act as a display of written, printed, or graphic matter upon the immediate container of any article. The term "labeling" means all labels and other written, printed, or graphic matters upon any article or any of its containers or wrappers, or accompanying such article.

Let's see. All right. The labeling of OTC drug product must provide enough information for the safe and effective use of the OTC drug product. For the safe and effective use, consumers engaging with the Drug Facts label must be able to self-diagnose, self-select, and self-treat. I'm going to go back to self-select. They not only need to be able to self-select, they also have to be able to unselect themselves from a particular drug product that is not good for them to use.

Sometimes an extra piece of labeling called a consumer information leaflet may be needed to provide supporting use information to the consumer. A few examples that we have of information that is communicated using a separate sheet of paper, which is a consumer information leaflet, let's say, for instance, weight loss products, there's another set of instructions that go with that. We also have additional information about how to quit smoking for the smoking cessation products, and then also the OTC inhalers have an insert like that, an insert or consumer information leaflet. There are others. Those are just a few examples.

Let's see. So other labeling under Part 201 that are not Drug Facts labeling are also required as appears in the gray text on this slide, a number of line items. I'm not going to be talking about those to you, but I just wanted to make you aware there are other labeling considerations we have to consider in over-the-counter drug products. It's the text in the red font that I'm focused on. 21 C.F.R. -- I should say Code of Federal Regulations, that's C.F.R., Part 201.66, which is entitled the Format and the Content Requirements for Over-the-Counter (OTC) Drug Product Labeling.

Something I'm not going to go into detail about for the

purpose of this presentation is to, oh, is to let you know that OTC drug products marketed in the United States are marketed under two different regulatory frameworks. A lot of folks don't know that. There are those OTC drug products marketed under approved new drug applications, or NDAs, and OTC drug products marketed under FDA's OTC drug monograph system that contain active ingredients found by FDA to be generally recognized as safe and effective, or GRAS. All OTC drug products are required, both regulatory pathways are required to be labeled with a Drug Facts label, as specified under 21 C.F.R. Part 201.66. Again, picked out in red on this slide, the regulation is entitled as you see it.

Okay. So getting back into the nitty-gritty of the history, in the *Federal Register* of March 1999, FDA published the OTC Drug Facts label regulation codified under 21 C.F.R. 201.66. And I'm also going to mention that the *Federal Register* is the daily journal of the United States government. It is online these days, and you may subscribe to receive it electronically. Some folks aren't aware that people actually read that and where to find it. This regulation under 21 C.F.R. 201.66 requires OTC drug products to comply with specific format and content requirements. For those of you

who do not read some part of the *Federal Register* almost daily, as I do, I provided this image, a half-page pullout of the actual page announcement from the *Federal Register* in 1999 telling the public that the Drug Facts final rule is available.

Three key points. This is about 50 pages long, but they were able to summarize all the points and conversation made in the 50 pages in a paragraph called the summary, which is right there in the left bottom corner of that page. And so the three key points that are announced to the public was that the rule standardizes the format and content requirements of OTC drug product labeling and assists consumers in reading and understanding OTC product labeling, and it assists in the safe and effective OTC product used by consumers. It also let manufacturers know that they were allowed to use up their stock of old labels, which I'm sure were considerable. The OTC labeling rule applies to more than 100,000 OTC drug products, which I've mentioned before, marketed under approved NDAs or the FDA OTC monograph regulatory system.

The Drug Facts label is patterned after the Nutrition Facts label. I show this side by side so you can see the relative similarity between the two.

So you may ask how did we inform ourselves about how to do this. It was a public process via public comment and public rulemaking. FDA received substantial input from consumers, industry, health professionals, and other experts in developing the format and the provisions delineated under the 1999 Drug Facts labeling final rule. You won't believe this, but the Agency received over 1,800 separate comments to the proposed rule. And I wasn't there at the time, but I've been through a similar process, and we read every single comment, and we respond to every single one. Sometimes they have several categories, and we lump them together, but we respond. Several public meetings were held, conducted consumer research, and FDA at the time met with many interested parties to obtain their input in this initiative, similar to this public meeting here that's taking place.

So this image is, this image, the green one that says simplicity, was one of several public service pieces the FDA produced to introduce the Drug Facts label. In its simplicity, the easy-to-read format and the Drug Facts label helps consumers choose the OTC medicine that's right for them.

So this is another -- this image is another image that I can't take credit for. The office that does this sort of

thing produced this as another public service. All nonprescription OTC medicine labels have detailed usage and warning information so consumers can properly choose and not choose the product and how to use the products. The information appears in order. Along with standardized format, the label uses plain speaking terms to describe the facts about each OTC drug. For example, "uses" replaces the word "indications," while other medical or medical technical words like "precautions" and "contraindications" have been replaced with more easily understood words and phrases. The label also requires a type size large enough to be easily read. And I'll pause here. I know you've probably read OTC Drug Facts labeling, and you probably think it's arguable about whether you can read it or not. But that's what I'm saying here. And specifically, details such as bullets, how to use those bullets, the spacing between lines, and how to make a clearly marked sections and improved readability. And I want to emphasize that, at the time, it was a considerable, considerable improvement over what had been available to the public previously.

So next, next page is the warnings. And the warnings communicate when not to use the product, conditions that may

require advice from a doctor before taking the product, possible interactions or side effects, when to stop taking it, when to contact a doctor, if pregnant or breastfeeding, advice is to contact a health professional for guidance, and of course, warnings to keep the product out of children's reach.

This is the last page about this. The last three items on the Drug Facts label are directions, other information, inactive ingredients. The directions will focus on the specific age categories, how much to take, how to take it, and how often and how long to take it. The other information section will tell you how to store the product properly and then certain other required information; there's some other things that can go in that spot. The inactive ingredients are listed here, substances such as colors or flavors or what a lot of us would know as excipients, the not active part of the product.

I'm about to wrap up here. Last part are that Drug Facts labeling gives you the format requirements, so it includes specifications for type size and style, which words can be bolded, what can be bolded, it's all supposed to be left-justified, what the leading is, and that's the space between two lines of text, other spacing, which letters can be

uppercase and which ones can be lowercase -- this part is extremely prescriptive -- and where graphical images can interrupt the text. There are bullets mentioned, barlines and hairlines, and hyphens. And you're wondering how can you do this kind of work. I just really love it. Use of more than one labeling -- I really do -- use of more than one labeling panel, modified formats for small packages, it's all described there.

Okay. So, you know, I didn't talk about the topic of the hour here of the whole couple of days, this nicotine-containing OTC drug products. It really wasn't the purpose of my talk, but I know you're probably wondering. So DNDP manages the OTC nicotine replacement therapies for smoking cessation, approved labeling. It also includes consumer information labeling, I believe, for all those products. Approved labeling that you want if you're curious and want to read to see what we've done is available to the public on our website, Drugs@FDA. It's fairly accessible, I think, on the website, pretty easy to find if you go there. So, again, you could look at the approved labels there.

I want to thank you. And here are the resources that I thought might interest you. We have a guidance labeling OTC

human drug products that's a Q and A. It was developed based on a lot of questions from industry about how in the world to implement the drug facts format and some of the finer details that needed clarification. You can find the Code of Federal Regulations through going usually to almost any government website, but I think you can get it through regulations.gov online. Because I rarely use paper anymore, it's really, you know -- you go. And the most recently approved labeling for nicotine-containing drug products may be found by searching Drugs@FDA. And I know this may be up later -- we're not going to do any individual slides. It's just the -- all right. Well, you probably may not need to do this website because I think if you -- am I supposed to say Google? You know, you can Google anything here and find it.

So that concludes my presentation, and I thank you for listening.

(Applause.)

DR. DRESLER: Okay. So Mary Brady from the Center for Devices and Radiologic Health will now be speaking on Labeling Initiatives at the Center for Devices and Radiologic Health.

MS. WEICK-BRADY: Right, left, okay. Thank you. Okay. I am Mary Brady. Thank you for sticking with us this afternoon.

I know it's been a long day for you, and I hope we all make this valuable for you for having to stick around. Again, I'm Mary Brady, and I'm in the Office of the Center Director in the Center for Devices and Radiological Health. I am working on the labeling initiative. We are not as far as drugs when it comes to the labeling initiative, but we are working on it, and I'm going to share with you the things that we've been doing. Let me mention that I do not have a vested interest in anything that is being discussed today.

Okay. We need to get out of there and move on. Okay. This talk is going to go over three different areas: The major activities that we are doing for a standard content of labeling, and this will be from 2010 to the present. I'll also talk to you about the research and findings that we had for a standard content and a web posting of labeling. And then I'm also going to briefly go over what we call the unique device identifier for device labels.

So our recent activities from 2010 to present. Understanding that there are tens of thousands of medical devices out there, we began our recent activities by reviewing what devices and biologics and drugs had done in the past. We mapped versions of standard labeling in existing documents,

including the Physicians Labeling Rule. Our Office of In Vitro Diagnostics has a rule in place for a standard content of labeling. We also looked at the Global Harmonization Task Force standard content of labeling and also our premarket approval group, who has a policy for what they want in labeling. We reviewed standards that pertained to labeling. We looked at adverse events. We looked at recalls. And we also got input from our division directors and asked them what they wanted in their particular medical specialty, whether it was implants, whether it was cardiovascular, dental, orthopedic, whatever. We did ask them for their input on that.

And after further discussion, we decided because of the high complexity of medical device labeling, we needed to start with a guidance to look at a standard content and not go down the regulatory route right away, understanding that we could miss some information if we just went down the regulatory route. And you know that when you write a rule, it stays in place for a long time, and it's very long to write in the first place. We presented this information at workshops in 2011, which was an Access to Labeling workshop, and also in 2013, which was a Standard Content and Format of Labeling.

So the other things that we have done, we announced a labeling repository as part of the home use initiative. And this was done back in April of 2010. We had five different pieces of this initiative for home use, and one of them was to get a labeling repository up for people like lay users and healthcare practitioners who work outside of clinical environments to access labeling because it tends to disappear once it gets outside of a clinical environment, and sometimes even in the clinical environment.

We discussed this with the National Library of Medicine. They do have the DailyMed site up there for the drugs, and we wanted to have something similar for that for devices. And they said, yes, we could do something like this. We talked to our Registration and Listing group because under statutory authority, this is where we can do this, under Registration and Listing. We talked with the Unique Device Identifier folks. And I'll tell you a little bit about Unique Device Identifiers in a little bit. But they also wanted to get their labels up on a website. And we felt that if we worked with them, we could do something in conjunction with them. And then we also talked to our FDA Gateway people, because that is where labeling is coming in for drugs and biologics

right now, and then that gets parsed over to the DailyMed site. So we worked with them also.

We then finally looked at different terms, some that are defined by regulation and some that are defined only by guidance. And we found that we had a bunch of different definitions like contraindications, warnings, and precautions that were not defined by regulation. They were only defined in guidance and somewhat inconsistently. So we are working at standardizing some of those definitions.

Now I'll go on to the research. The first thing that we did for research for a standard content of labeling was to work with the Research Triangle Institute for 2 years. And we had a two-phase study. We did a focus group of about 100 healthcare practitioners asking them what they wanted in labeling, did they care about labeling, do you even look at labeling, and when you go looking in the labeling, what do you look for, what are the pertinent things that you're looking for, and how would you want to access that labeling. Amongst other findings, they did tell us they want a standard content of labeling. They don't want to go looking through a 650-page document to find where the warnings are, and they want them all in one place. They also said they don't have time to look

at a lot of the full content of labeling, and they want an abbreviated form of labeling, which is very similar to what we have for the highlights section for drug labeling. And they also said they would prefer to access it electronically, if possible.

With that in mind, then, we did go down checking out a prototype of three different types of infusion pump labeling, only looking at the abbreviated version to see if we could get device labeling into an abbreviated version. So we did a second phase of that study, and we asked 600 healthcare practitioners to react to one of those three prototypes of labeling. And of all three of those, they were happy with either one of them. And they found that the sections were good, they were well defined, that there was good white space, there were good diagrams. So we did get a positive reaction to that second phase of our research there.

Another thing that we did was a Cooperative Research and Development Agreement. And that's called a CRADA. We affectionately call that a CRADA. And it was with Kwikpoint. And this is a company that does visual language development. They work a lot with the Department of Defense and the World Health Organization to crosscut all sorts of language barriers

when having instructions for use for something. Our question to them was is visual language a substitute for some instructions for use? And we chose two different devices that seemed quite innocuous yet were causing a lot of problems. They were causing both injuries and deaths. And this was a use of sharps and sharps containers, and also with patient lifts. After they went through this, we did find that, yes indeed, with good usability testing, you can substitute visuals for some text. This is not in regulatory mode at this time. This was just something that we were checking to see if we could actually do.

These are the examples of the Patient Lifts Safety Guide that we have, and these are online. And then we had a smart -- Be Smart With Sharps brochure that come out from that.

Another thing that we did, and I think this might pertain a little bit more to what's going on with e-cigarettes, was we talked to the Caregiver Action Network. And these were 120 surveyed participants and their caregivers only and laypeople, and we asked them what they wanted in labeling, how did they look for labeling, where did they find it, what were the important pieces of labeling for them. And what we found was that their responses were very similar to what the healthcare

practitioners had said. In addition, though, and this is important, was that they needed to know how to clean products, they needed to know what to do with the battery after they were done using, they needed to know how to maintain the product, and they also needed to know how to dispose of the product.

With this in mind, then, we also are doing a study through our Entrepreneurs and Residents Program, and it's funded by our Critical Path Program. When we had the workshop last year in 2013, one of the public speakers said, look, you've done a good job with the research so far. What you are missing is taking that draft standard content of labeling and checking it against existing labeling to see if it really is more useful and usable. Is this something that is going to work for people once you get out there? So with that, this is our third phase of the labeling study. We have three social scientists that are working as special government employees, and they're helping to develop this protocol. This will be a cognitive test. We are going to develop scenarios with our draft content of labeling and do it against existing labeling, and these are being brought in through material transfer agreements with different people from industry. And we will

see if they can find information based on these scenarios, if they can find that information easier in one or the other. Hopefully, we'll have 6 to 10 different devices, and we will also be working in the hospitals and checking on a couple of devices that they have and they were willing to work with us.

Okay. Now I'm going to speak a little bit about the Unique Device Identifier, or UDI, for just a few minutes. It covers the label for the device, which is the carton, the package, the box, or anything that contains a medical device. This is a new law, and the first devices in the final rule are now subject to submitting their information to FDA. This started in September. This, of course, is a cursory review of UDI and is not meant to be a tutorial. I'll gladly refer you to the UDI staff for more information if you want to know about that.

So there are two requirements for UDI. The first is that the label of every medical device must have a Unique Device Identifier. There is guidance for manufacturers to determine what constitutes a UDI and what they can put on their product. The second requirement for UDI is that the labeler of the device must provide the information needed for each version or model of their products that need a UDI. And I want to note

here that there are devices that are exempt from regulatory review by FDA, and they would not require a UDI.

This is an example of a device label and what the required elements are for the label. So the UDI here is that little barcode on the bottom. That is called an automated information data capture. And this is the barcode. And the piece underneath it is the human readable interpretation, and that's the numbering system. So you have to have both of those pieces. The UDI, the barcode itself, is made up of two parts. You have the device identifier, and that is what is assigned to a particular version or model of that product. And you also have the production identifier in there, and that indicates how the manufacture of the device is controlled or managed, and that could be by lot number, by serial number or expiration date, or whatever it would be. You also have to have the brand name of the device and a catalogue number on the label. You also must provide whether or not it is for single use, and you also have to provide storage and handling instructions. They're allowed to use symbols with adjacent explanatory text to explain any of these things, knowing that there's minimal real estate on some of these devices. And then, finally, you have to have the labeler's name and

address.

Okay. This information comes from the FDA's system called the Global Unique Device Identifier Database. And we called it GUDID. So all of this information does come into FDA at CDRH, and we look through this information. I'm just showing you a screenshot here of what comes out, or what comes to us, I'm sorry, and how they separate the information. They have identification elements, and then they also have the patient safety elements. This should be available, I believe, in the spring for public use so you can search through it. They're working on that right now.

Finally, we believe the key benefits of having a Unique Device Identifier for us will help us to more accurately get reporting and reviewing and analyzing of the adverse event reports that come in. We believe it will help us reduce medical errors for device users because they'll be able to more rapidly and accurately identify a device. We believe that documenting the device use would be beneficial in electronic health records and registries. We think we can more effectively manage device recalls this way. And we also believe we can address counterfeiting and prepare for medical emergencies in an easier way.

And with that, I want to thank you, and I'm going to hand it over to Ken.

(Applause.)

DR. DRESLER: Okay. Labeling Considerations for Battery-Powered Devices. Ken Skodacek -- I think I'm getting it -- from the Centers for Devices and Radiologic Health. Bring us home.

MR. SKODACEK: Thank you for sticking with us this afternoon. Again, my name is Skodacek. I'm with Center for Devices and Radiological Health. I'm a policy analyst in the Office of Device Evaluation and also Co-Leader of the Center's Battery Working Group. You're going to notice that a lot of my slides are similar to the slides earlier today, but I promise you to make them just as interesting.

So why is labeling important? As you listen to my presentation now, I want you to think about how labeling might improve the safety and performance of the device rather than just focusing on the design and manufacturing.

I'm an FDA employee and still have no relationships or financial interests to disclose.

So why does the FDA care about labeling for battery-powered devices? As I mentioned earlier, FDA does not

regulate batteries, but FDA does regulate medical devices, and batteries are one of the critical components in those devices. Failure of the battery can result in catastrophic consequences and failure of the medical device. The labeling is one way to improve the safety and performance of the device. And as the first speaker mentioned, I'm referring to labeling in a broad sense, not just what FDA would consider as labeling, but anything that ultimately helps the end user use the product in a way that's going to function well.

So, again, as an electrical engineer, this is the symbol for a battery. A battery seems so incredibly simple, but in fact, it's a very complex component. The available voltage and current may vary depending on the design and manufacturing characteristics and how much quality control is put into the manufacturing, as well as the load, the temperature, the storage time. Maintenance is critical to the safety and performance of batteries and battery-powered devices, especially for those devices that use rechargeable batteries. Misunderstandings or inaccurate and outdated understanding of how rechargeable batteries should be used is one of the things that limits their performance.

So what could go wrong with a battery-powered medical

device? Before we get into the examples earlier today, I want you to think about how labeling could have presented these issues. And I apologize that I don't have too many shocking, jaw-dropping examples, but I promise to add to them.

So I'm going to present some of the other points that we have learned, and I wanted to clarify that labeling is not the first or primary way of reducing frequency or severity of issues. Rather, labeling could be used in addition to these other remedies or methods. So, again, this is the recent story from a local newspaper here. About 5% of all adverse events and reports sent to FDA are related to batteries, and about 75,000 events over the past 3½ years are related to the battery.

In addition to this example, I wanted to present another one. So there's actually an automated external defibrillator that allowed you to use off-the-shelf consumer batteries much like D cells. And this device, when you plugged it in, it actually charged the batteries through the device. But in fact, the end user could potentially use non-rechargeable batteries. So they put the non-rechargeable batteries in the device, plug it into the wall, and can you imagine what happens? Those batteries overheated and exploded and actually

caused a fire within the institution.

Another example here, of course, is the electronic thermometer that actually I presented earlier today. I'd like you to consider that labeling could have been placed on a device, including an expiration date that maybe the battery is getting close to depletion because it's been in there for a while or even a reminder to the end user that the temperature reported may be inaccurate when the flashing light is reporting that the battery is low.

In the example of the exploding electronic toothbrush, labeling could have been included on the device to remind the user that -- to ensure that the one-way vent hole remained clean and clear, and labeling could have been included to remind the user to just select the appropriate replaceable batteries of certain brands or manufacturers which might have been less likely to release the final gas.

In regards to the sinus irrigation system, again, this is something you rinse your sinuses out with, where it could have been the saline solution mixed with the battery compartment. There could have been something for the user to remind them to replace the saline solution on a regular basis or to replace or check the batteries on a routine basis, preventing the

issue.

So, again, in order to proactively address these issues, FDA founded the Center's Battery Working Group. Our mission and objectives are here. We had a public workshop. Again, around 700 different people came to this workshop. We actually did have Kwikpoint present at the workshop as well, and what we found is that people were very interested in finding new ways to put graphical labelings either with a device or actually on the device itself to remind the users how to use the product properly.

Now, I wanted to emphasize an important point. For medical devices, proper operation and maintenance of the device by the healthcare provider or patient is critical to the operation of that device. Even if you as a manufacturer develop the perfect device, there is the potential for serious malfunction when the user does not select an appropriate battery or does not properly maintain the device. This is especially important when the end user can purchase batteries manufactured by a third party, and to explain this point, I'll tell you a little story on a subsequent slide.

What are some of the concerns we have experienced with medical devices? Surprisingly, it's poor maintenance that

causes most of the significant problems. A fully depleted battery can be damaged during the depletion process. So if you have something that's been sitting a while -- I don't know if anyone's had a laptop that might have been sitting in a closet, and you try to pull it out and charge it up, and it actually doesn't work at all. So rechargeable batteries, once they're depleted beyond a certain point, they no longer function.

Recharging that battery can then result in overheating and fires. Another issue that we found is that labeling wasn't easily accessible to users. Manuals and instructions are frequently discarded or lost, and one method of addressing that issue is to print the essential instructions directly on the device or on the case, or to connect the instructions to the device much like you see on a pillow, where it has the label on there, and you kind of have to rip it off before you use it. And, of course, many children's products also use this method.

As I mentioned earlier, the CPSC, again coincidentally just one day before our battery workshop, sent out a notice warning consumers about selecting the appropriate batteries and chargers for use with their smartphones. Now, I have to

admit, I'm also guilty here. I bought an inexpensive car charger for my iPhone. It costs five dollars at the dollar store, and of course, I was using it in my car, and eventually, the wires frayed and shorted out, and I had a smoking wire charger in my car. So even I'm guilty of that, and I'm part of the Battery Working Group.

So how is this discussion about labeling relevant to e-cigarettes? Well, here are some claims I obtained from just one website from a manufacturer. If you read these claims, you can see how an e-cigarette manufacturer might make claims which are sometimes included in the labeling. For medical devices like life-sustaining devices, maybe a pacemaker, or other consumer products like laptops, there's an interest in making a fair comparison between devices, and I invite you to consider how this issue might be addressed for the devices that we're discussing as part of this workshop.

In addition, in preparation for this presentation, I did some searching online. And as you can see, back in mid-2013, the electronic cigarette market was about 75% or 72% disposable. And I'm not sure if it's going up or down, but if you notice, most of the manufacturers now offer a variety of different devices with disposable and rechargeable batteries

or rechargeable battery packs.

Regarding the third-party battery manufacturers, I have another little story, a personal story that I'd like to share with you. So I recently bought a camera, a digital camera before I was going on a trip internationally. And I wanted to make sure that if I was out taking pictures, that I could have enough battery to take those pictures. But, of course, when I searched online for the battery for that particular camera, it cost about 50 to 75% of the total cost of the camera, and I thought that's just ridiculous. So what did I do, again, as a member of the Battery Working Group? I searched on Amazon, found another third-party manufacturer that was selling batteries for about $1.99. I bought five of them for 10 dollars, and I figured even if one of them works, I'll be lucky. But, again, I wouldn't recommend that, because you don't know what you're getting when you buy something -- a battery for a digital camera for $1.99.

You also might consider the storage and use conditions. So I don't know if anyone looked outside, but it's snowing today. And the performance of a battery varies widely depending on the individual temperature. So if you were to be using, say, an e-cigarette in an environment like where it's

cold out today and it's 30 degrees, and you have that e-cigarette set with certain specific settings for how much nicotine it's going to deliver, and then you take that same product and you travel to, say, Florida, you're going to go on vacation, you put it in your pocket, you get on the plane, you arrive in Florida, and it's 90 degrees, the fact is is the operation of that device might be very different.

So as I conclude my presentation, I suggest that you consider the question, how would labeling improve the safety and performance of e-cigarettes?

Thanks again for your time and attention, and I acknowledge my colleagues and some references. Thank you.

(Applause.)

DR. DRESLER: Okay. Well, thank you to the speakers for that last panel. It's always hard being in the last panel, so thank you very much for such a nice set of presentations.

To the people who are still in the room, thank you. It is a smaller group than we started out with either yesterday or today, but, you know, thank you for hanging out here. I will say on behalf of the FDA, we're very grateful to have this information that has been presented, both the scientific presentations, the panelists, and the public comments. So

thank you so much.

I did receive with the last speakers -- we don't have a panel for addressing questions from that, but let me just remind everyone, there is a docket that's open, so go ahead and put your comments, certainly scientific data and comments and concerns into that docket.

I did not know it was snowing outside, so as we conclude, please drive safely, and thank you very much, and we'll see you at the next workshop.

(Whereupon, at 3:09 p.m., the meeting was adjourned.)

C E R T I F I C A T E

This is to certify that the attached proceedings in the matter of:

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were held as herein appears, and that this is the original transcription thereof for the files of the Food and Drug Administration, Center for Tobacco Products.

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